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THIRD SERIES FOUNDED BY EDWARD JACKSON

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OPHTHALMIC SUSPENSION

When severe ocular inflammation threatens vision, Prednefrin Forte provides the therapeutic potency needed for effective control . . . in cases where other topical preparations have failed.

What makes Prednefrin Forte so effective?

Prednefrin Forte is the most potent topical preparation you can use—it contains prednisolone acetate in a concentration of 1.0%. Furthermore, the prednisolone is presented in an extremely fine, aqueous suspension (the particles are approximately half the size of a red blood cell). Because the special suspension remains in the eye for a prolonged period after instillation, a repository-type dosage is obtained. Anti-inflammatory action is continuous and uniform—patient response, even in the most severe anterior segment inflammatory condition, is often seen within hours.

FORMULA: *Prednefrin Forte Contains . . .*

Prednisolone acetate	*1.0%*
Phenylephrine HCl	*0.12%*
Methylcellulose	*0.12%*

DOSAGE: *1-2 drops in the conjunctival sac two to four times daily. During the initial 24-48 hours the dosage may be safely increased to 2 drops every hour.*

SUPPLY: *In 5 cc. plastic dropper bottles — on prescription only.*

UNSURPASSED POTENCY FOR OCULAR INFLAMMATIONS BEYOND THE CONTROL OF ORDINARY STEROID STRENGTHS

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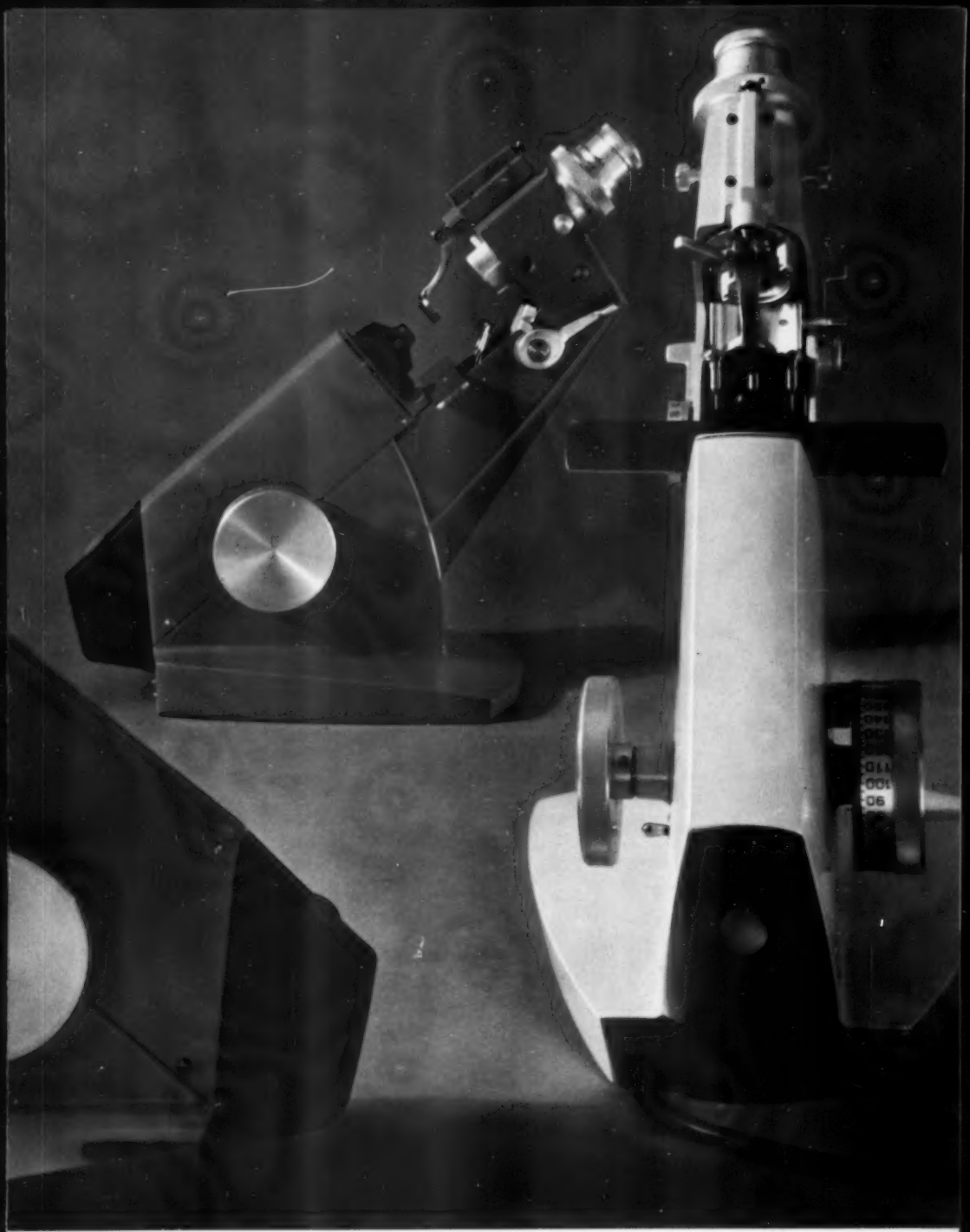

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Filter swings out of optical path to let you measure the darkest of outdoor lenses. You have illumination to spare . . . no need for bothersome step-up transformer.

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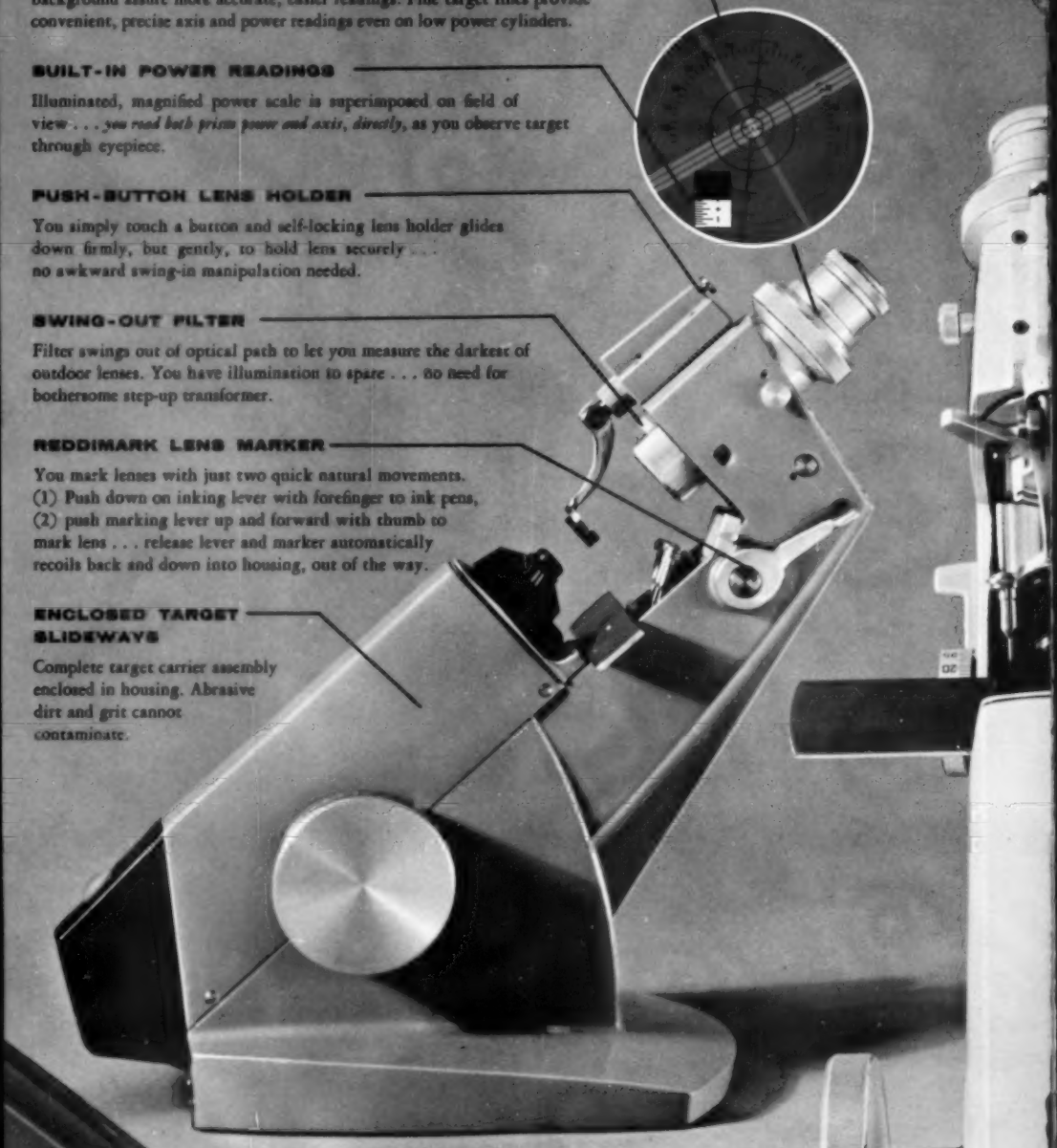
ENCLOSED TARGET SLIDEWAYS

Complete target carrier assembly enclosed in housing. Abrasive dirt and grit cannot contaminate.



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clinical photographs

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INDICATIONS: Trauma—mechanical, chemical or thermal; inflammation of the conjunctiva, cornea, or uveal tract involving the anterior segment; allergy; blepharitis.

CAUTION: Steroid therapy should never be employed in the presence of tuberculosis or herpes simplex.

NeoDECADRON is also available as the ophthalmic ointment (.05%). Ointment and solution are available with dexamethasone 21-phosphate alone: DECADRON® Phosphate Ophthalmic Solution and DECADRON Phosphate Ophthalmic Ointment.

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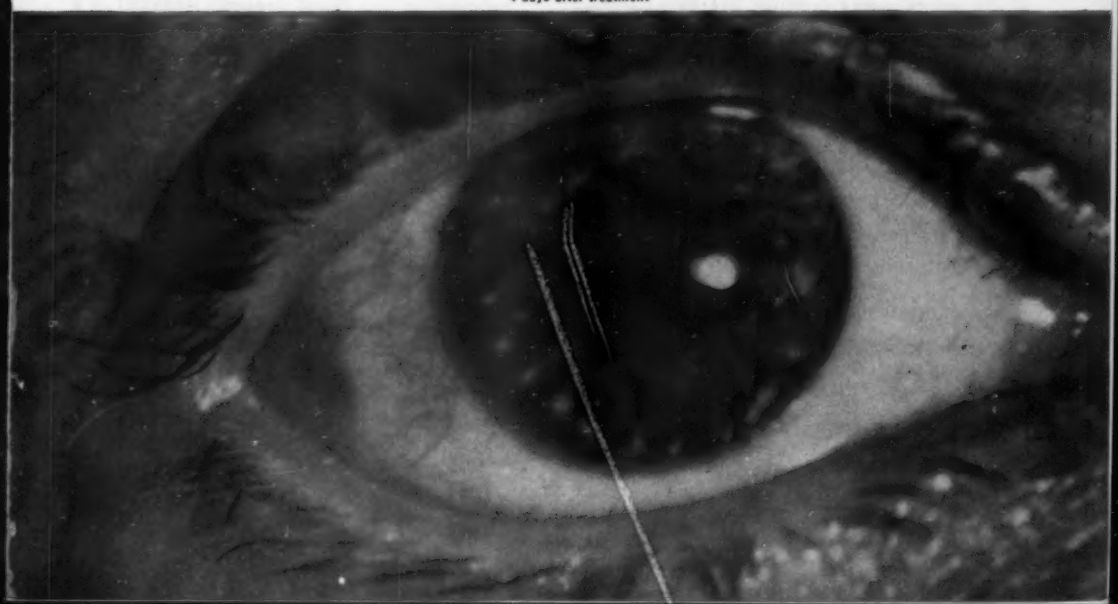
4 days after treatment



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A 30% urea—lyophilized and highly purified—in combination with 10% invert sugar (TRAVERT®)

IN ACUTE ANGLE CLOSURE GLAUCOMA—

"dramatic response"

IN PREPARATION FOR INTRAOCULAR SURGERY—

"effective in cases in which carbonic anhydrase inhibitors had little or no effect"

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In 15 of 26 scleral buckling procedures "its use was definitely helpful."

IN ORBITAL SURGERY—

"orbital exploration has definitely been facilitated."

Reference: Javid, M., and Davis, M.: Scientific Exhibit No. 922, A.M.A. Annual Meeting (June) 1960.

Information You Would Request: UREVERT is a special modification of an old agent—urea. The specifications—30% urea, lyophilized and highly purified, in combination with 10% invert sugar (TRAVERT*)—were found to be optimal by researchers at the University of Wisconsin Medical School. More than four years of basic and clinical study have firmly established the value of UREVERT as the preferred agent for brain decompression, and now to reduce intraocular pressure.

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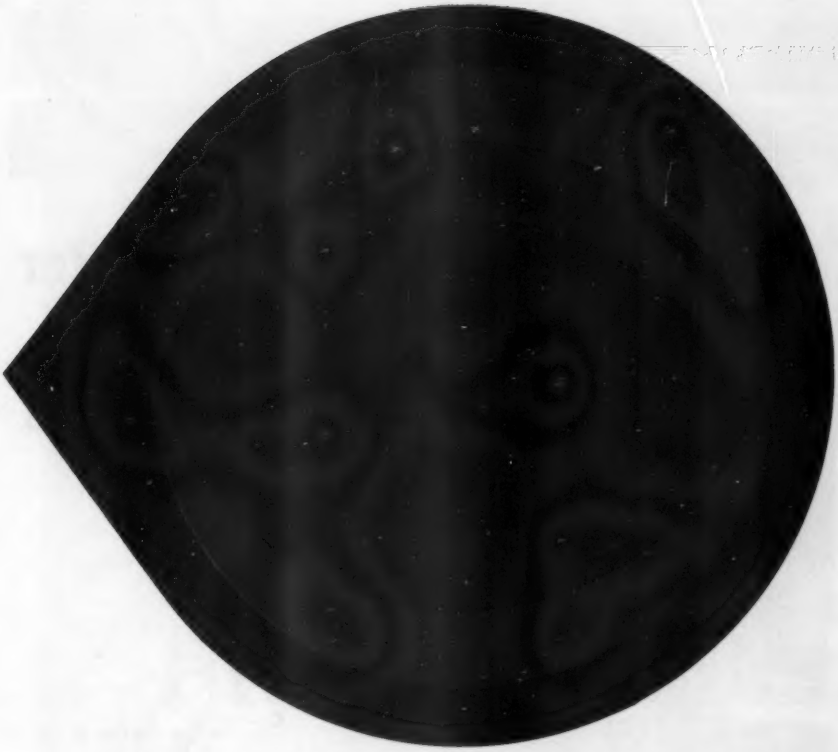

THE DRUG THAT REDUCES INTRAOCULAR PRESSURE EVEN IF MIOTICS AND CARBONIC ANHYDRASE INHIBITORS HAVE FAILED

Indications: UREVERT has proven to be extremely effective in reducing intracranial pressure preoperatively and postoperatively, irrespective of cause. Recent evidence shows that UREVERT will reduce intraocular pressure even when miotics and carbonic anhydrase inhibitors fail. It has been used with success in acute angle closure glaucoma, preparation for intraocular surgery, retinal detachment surgery, orbital surgery.

Dosage: Intravenously, one gram urea per kilogram body weight at rate of approximately 60 drops per minute.

Repeated Administration: 1. Careful recording of fluid intake and urinary output. 2. Maintain a positive water balance. 3. Maintain electrolyte balance and observe B.U.N. *Note:* In all cases under general anesthesia an indwelling catheter is necessary.

Contraindications: 1. Severe renal damage. 2. Active intracranial bleeding. 3. Marked dehydration.

Caution: 1. Keep needle securely within lumen of vein to avoid extravasation. If pain at site of injection, relieve by injection of 0.5 cc. of 1% procaine through same needle. 2. Lower extremity infusion in older patients.

Side Effects: Headaches may occur in patients with normal intracranial pressure from marked lowering of intracranial pressure. Keep patient flat in bed for duration of UREVERT administration and subsequent 2-3 hours.

REFERENCES: 1. Fremont-Smith, F., and Forbes, H. S.: Arch. Neurol. & Psychiat. *18*:550 (Oct.) 1927. 2. Javid, M., and Settlage, P.: J.A.M.A. *160*:943 (March 17) 1956. 3. Javid, M.; Settlage, P., and Monfore, T.: Surgical Forum 7:528, 1957. 4. Javid, M., and Settlage, P.: Tr. Am. Neurol. A. 1957, pp. 151-153. 5. Javid, M., and Anderson, J.: Surgical Forum *9*: 1959. 6. Javid, M.: Surg. Clin. North Am. *39*:907 (Aug.) 1958. 7. Javid, M., and Anderson, J.: J. Lab. & Clin. Med. *53*:484 (March) 1959. 8. Stubbs, J., and Pennybacker, J.: *Lancet 1*:1094, 1960. 9. Tench, J. H.; Javid, M., and Gilboe, D.: Anesthesiology *21*:117 (Jan.-Feb.) 1960. 10. Javid, M., and Davis, M.: Scientific Exhibit No. 922, A.M.A. Annual Meeting (June) 1960.

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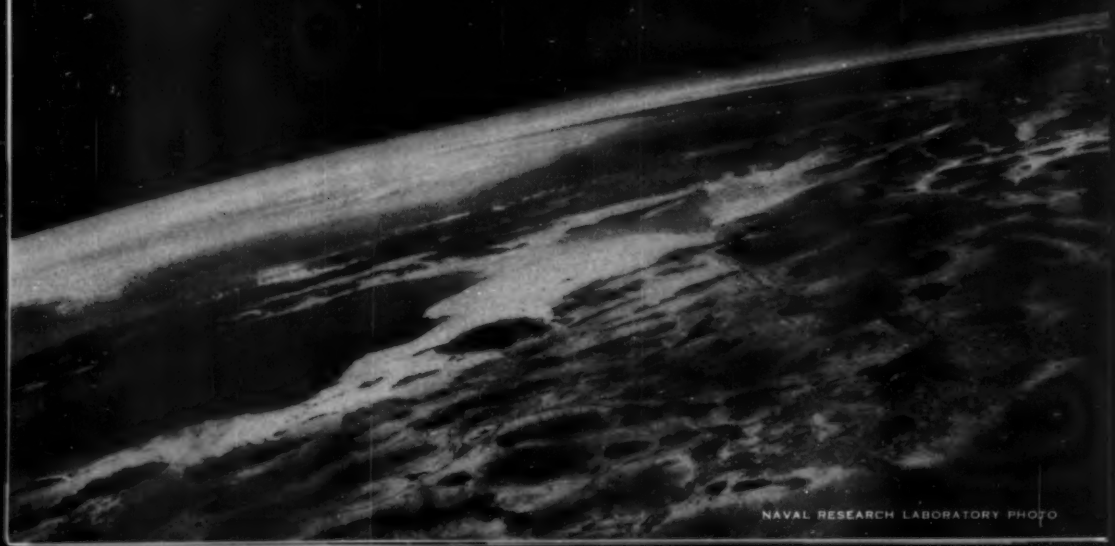

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Alpha CHYMAR®

ALPHA CHYMOTRYPSIN

Alpha Chymar offers an outstanding advance in technique over mechanical zonulysis. Many thousands of lens removals have been made easier through use of this agent, which dissolves or greatly weakens the zonular fibers so that the lens may be slipped out.[1-4] This simplified manipulation helps to avoid the incidence of capsular rupture and zonular traction on structures of the inner eye, often encountered during mechanical removal.[5]

Commenting on the ease of the technique, one operator has remarked that "alpha chymotrypsin still is far superior to any other technic I have ever used or have observed."[2]

1. Cogan, J. E. H.: Proc. Roy. Soc. Med. *51*:927, 1958. 2. Jenkins, B. H.: South. M. J. *53*:44, 1960; discussion by Raiford, M. B. 3. Raiford, M. B.: J.M.A. Georgia *48*:163, 1959. 4. Rizzuti, A. B.: A.M.A. Arch. Ophth. *61*:135, 1959. 5. Thorpe, H. E.: Am. J. Ophth. *49*:531, 1960.

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KANKAKEE, ILLINOIS
Armour Means Protection

***Alpha* CHYMAR**

For Ophthalmic Use

Alpha Chymar is a lyophilized form of crystallized alpha chymotrypsin, a proteolytic enzyme obtained from mammalian pancreas. The contents of the vial when reconstituted with 5 cc. of Alpha Chymar Diluent provide a solution containing 150 Armour Units per cc.—comparable to a 1-5000 dilution. ACTION AND USES: Alpha Chymar is specific for lysis of the zonule in lens extraction. The lytic action is a selective one that does not adversely affect the hyaloid membrane, lens capsule, or other intra-ocular structures. ADMINISTRATION: Used intra-ocularly. For suggested procedure in cataract surgery see package insert. CONTRAINDICATIONS: Until additional reports are obtained, the use of Alpha Chymar is not advised in children under ten years of age. SUPPLIED: Cartons of 5 packages—each package contains one vial of lyophilized Alpha Chymar and one vial of Alpha Chymar Diluent (Sodium Chloride Injection, U.S.P.). For special precautions regarding reconstitution and handling, see package insert.

CHLOROMYCETIN-POLYMYXIN OPHTHALMIC OINTMENT

(chloramphenicol-polymyxin ointment, Parke-Davis)

For Topical Therapy and Prophylaxis Against Many External Ocular Infections

■ Provides CHLOROMYCETIN for wide-spectrum antibacterial action against external ocular infections ■ Provides polymyxin B for additional protection against certain gram-negative organisms such as *Pseudomonas* and *Aerobacter aerogenes* ■ Helps prevent emergence of secondary invaders while ocular lesions heal.

In ophthalmic infections, both chloramphenicol and polymyxin have proved highly efficacious.[1] CHLOROMYCETIN penetrates either inflamed or noninflamed ocular tissues "...better than any other antibiotic, regardless of route of administration."[2] Moreover, CHLOROMYCETIN stands out among antibiotics because of its continuing effectiveness against staphylococcus,[3] a common invader in ocular infections.

With the incidence of gram-negative pathogens in eye infections on the rise,[4] polymyxin B would appear to be of particular value as a component of any preparation designed for therapy and prophylaxis in external ocular infections. The combination of CHLOROMYCETIN and polymyxin B in convenient ointment form thus provides a rational and effective approach to treatment.

CHLOROMYCETIN-POLYMYXIN Ophthalmic Ointment contains 10 mg. chloramphenicol and 5,000 units of polymyxin B (as the sulphate) per gram. Supplied in ⅛-oz. sterilized ophthalmic-tip tubes.

See medical brochure for details of administration and dosage.

References: (1) Perkins, E. S.: *Practitioner* **178**:575, 1957. (2) Queries and Minor Notes: *J.A.M.A.* **161**:1032, 1956. (3) Fisher, M. W.: *Arch. Int. Med.* **105**: 413, 1960. (4) Smith, C. H.: *Eye, Ear, Nose & Throat Month.* **34**:580, 1955.

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for topical therapy
of certain types of
GLAUCOMA...

...two highly effective miotics

HUMORSOL®

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•potent, longer-acting than other miotics •two instillations weekly are often sufficient to control glaucoma •because it is unusually potent, it may be uniquely useful in breaking up peripheral synechiae •aqueous—isotonic with conjunctival fluid •stable—refrigeration not required •0.25% ophthalmic solution, in 5-cc. bottle with dropper

FLOROPRYL®

Isoflurophate U.S.P.

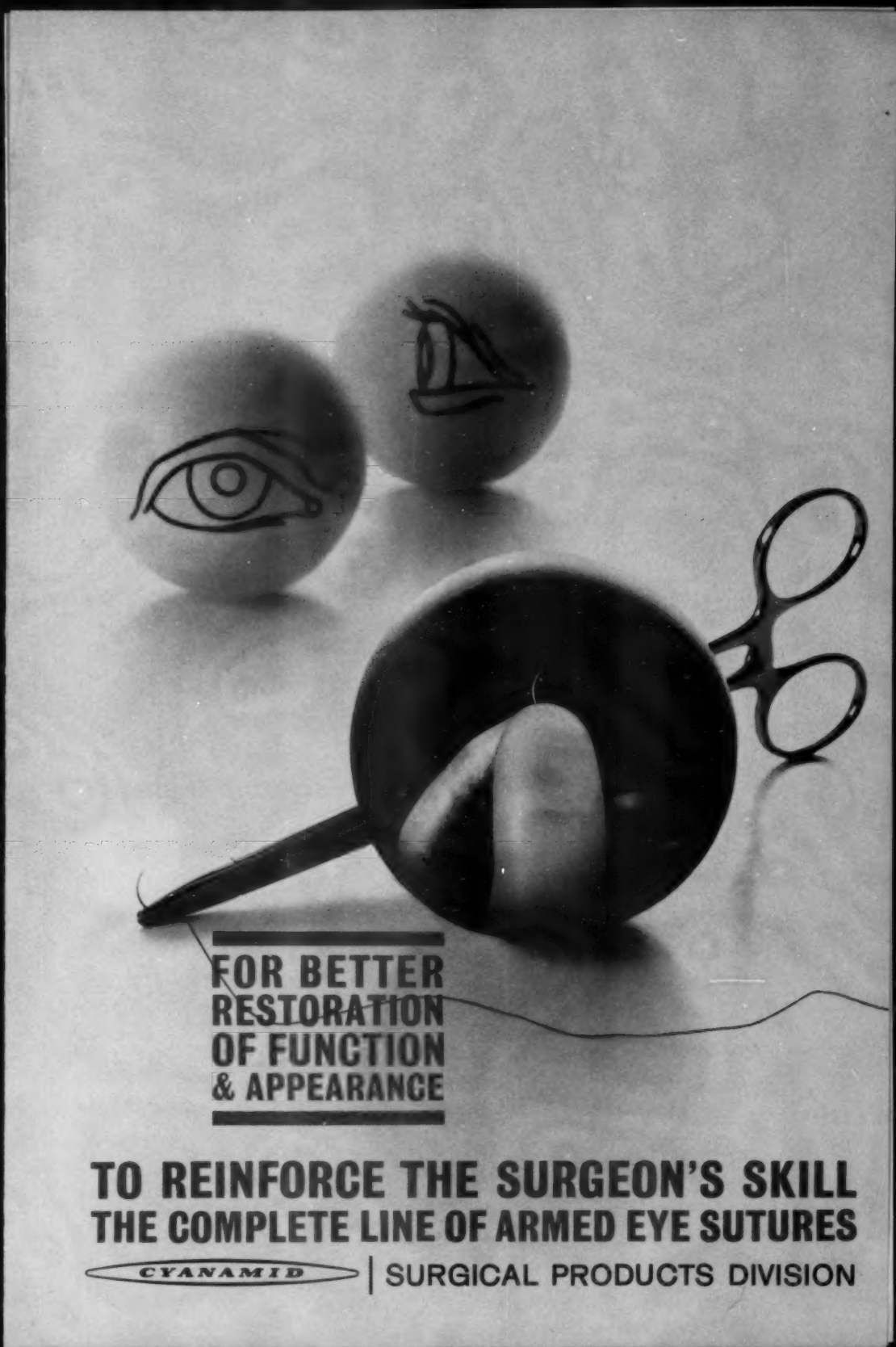
•long-acting—in glaucoma, one instillation daily is often sufficient; (in strabismus, one instillation every two days to one week) •may be effective when other agents fail •two topical dosage forms—0.1% ophthalmic solution in anhydrous peanut oil, in 5-cc. bottle with dropper; 0.025% ophthalmic ointment, in 3.5 Gm. tubes

also available: **DARANIDE®** Dichlorphenamide for oral control of intraocular pressure, 50-mg. tablets

Before prescribing or administering HUMORSOL, FLOROPRYL and DARANIDE, the physician should consult the detailed information on use accompanying the package or available on request.

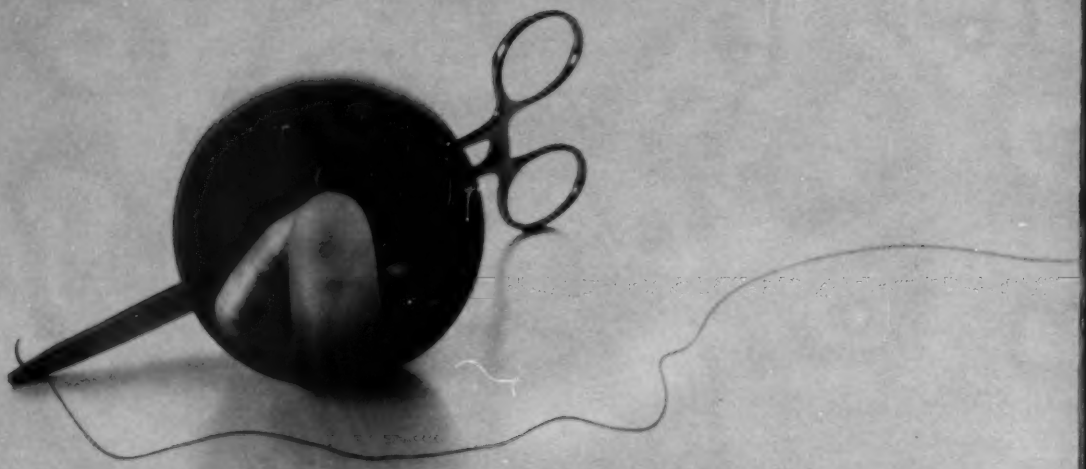
MSD MERCK SHARP & DOHME, DIVISION OF MERCK & CO., INC., WEST POINT, PA.

HUMORSOL, FLOROPRYL AND DARANIDE ARE TRADEMARKS OF MERCK & CO., INC.



TO REINFORCE THE SURGEON'S SKILL
THE COMPLETE LINE OF ARMED EYE SUTURES

CYANAMID | SURGICAL PRODUCTS DIVISION



OPHTHALMIC SUTURES WITH HAND-HONED NEEDLES FOR CORNEOSCLERAL PROCEDURES—

QUALITY EYE SUTURES FOR MUSCLE AND TISSUE SURGERY...

NEW SILICONE-TREATED SILK—physiologically inert silicone coating minimizes risk of fibroblastic and other damaging reactions. Silicone also helps protect against enzyme penetration and "capillary-spread" of bacterial infection. New construction significantly increases suture strength, permitting the use of finer sizes. The balanced "hand" provides greater handling ease in suturing and tying.

NEW HIGH TENSILE SURGICAL GUT—absolute uniformity of entire strand ensures greater knot and tensile strength. Satin matte finish creates a highly pliable suture strand with excellent knot-holding characteristics. Carefully controlled chromic processing maintains in situ gut strength during wound healing. Rigid laboratory digestion tests assure a uniform rate of absorption and compatibility with tissue. Also available are DERMALON® Monofilament Nylon and SURGILON® Braided Nylon sutures.

ATRAUMATIC® NEEDLES — new drilled end design permits uniform tempering of entire needle for greater strength. The needle holder may be placed far back on the needle shaft for greater tissue "bite". Flat surface opposite cutting edge is carried back on the needle shaft, assuring a firm grip in the needle holder.

All sutures are available in the safer, protective SURGILOPE SP® Sterile Suture Strip Pack—winner of the 1960 Packaging Institute Award for the most outstanding advance in applied packaging technology.

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IN EYE INFECTIONS

broad antibacterial range

effective anti-inflammatory action

OPHTHOCORT

chloramphenicol-polymyxin B-hydrocortisone ointment, Parke-Davis

OPHTHOCORT provides:

Chloromycetin® (chloramphenicol, Parke-Davis) for prompt, wide-spectrum antibacterial action[1-6]

Polymyxin B for additional control of gram-negative invaders, including *Pseudomonas aeruginosa*[1,7]

Hydrocortisone to decrease inflammation, reduce discomfort, and to lessen danger of tissue scarring[8]

OPHTHOCORT affords: wide-spectrum antibacterial, anti-inflammatory, and antiallergic action in ocular inflammation complicated by infection.

Each gram of Ophthocort contains 10 mg. chloramphenicol, 5 mg. hydrocortisone acetate, 5,000 units polymyxin B sulfate in a special base of liquid petrolatum and polyethylene. *Supplied* in ⅛-oz tubes. *Precautions:* Contraindicated in herpetic infections and ocular tuberculosis. When hydrocortisone is applied locally in treating bacterial diseases of the eye, care must be exercised to assure that the condition is not actually progressing while the external appearance improves. *See medical brochure for details of administration and dosage.*

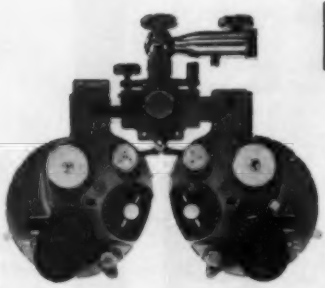
References: (1) Morrison, W. H.: *Nebraska M. J.* 45:106, 1960. (2) Perkins, E. S.: *Practitioner* 178:575, 1957. (3) Tassman, W. S.: *U. S. Armed Forces M. J.* 10:161, 1959. (4) Kamiya, S.: *Am. J. Ophth.* 42:269, 1956. (5) Holland, R. W. B.: *Arch. Ophth.* 57:214, 1957. (6) Benton, C. D., Jr.: *South M. J.* 51:1562, 1958. (7) Blakiston's New Gould Medical Dictionary, ed. 2, New York, McGraw-Hill Book Company, Inc., 1956, p. 945. (8) Ostler, H. B., & Braley, A. E.: *J. Iowa M. Soc.* 44:427, 1954.

99041

PARKE-DAVIS

PARKE, DAVIS & COMPANY, Detroit 32, Michigan

Lights attached to refractionist's hands show the wearying motion required to perform a simple refraction with a trial lens set and trial frame. Left hand takes three different sphere powers from trial case and inserts them in frame; right hand steadies the frame. Same procedure is repeated for three changes of cylinder power. Efficient? Compare the light paths in the two pictures.



LESS FATIGUE, LESS TIME PER PATIENT

Here the refractionist is using the Greens' Refractor for the identical procedure shown in the first photograph. The upper bright spot shows how the left hand remains in position for the six adjustments required to duplicate the trial lens changes. The lower bright spot shows the minimum motion required of the right hand to bring the retinascope into play for each change. This is a saving of time and energy.

Here's new light on how the B & L GREENS' REFRACTOR saves energy while you handle more patients per day

The paths of light in these authentic photographs tell part of the story. Here's visible proof of significant conservation of your vital energy, your limited time. It's readily apparent that the Greens' Refractor can help you treat more patients . . . and keep you feeling fresher at the end of your busy day.

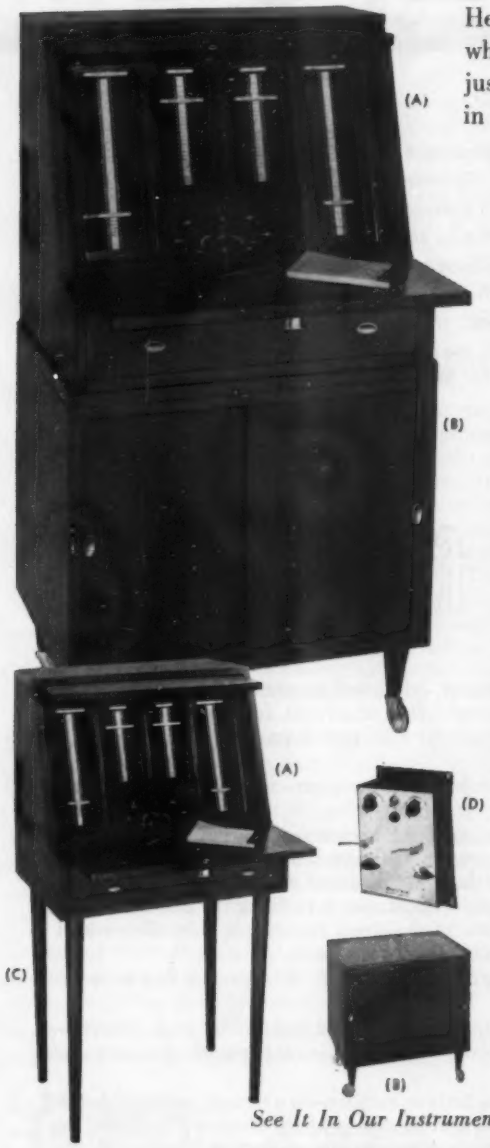
But what the photographs *can't* show is the higher prescription accuracy . . . the greatly increased visibility . . . the unequalled efficiency of operation . . . that give full scope to your professional skill. Only a demonstration can show you this. Call your Bausch & Lomb ophthalmic instrument dealer. Or write to Bausch & Lomb Incorporated, 91117 Lomb Park, Rochester 2, N. Y.

BAUSCH & LOMB

SINCE B&L 1853

Versatile · Beautifully Styled

New Visionette Lens Cabinet Ensemble



Here is an illuminated lens cabinet ensemble whose compact convenience is designed to adjust to almost any office space. Modular styled in grained walnut or light birch finish.

- Lens cabinet (23" wide x 21¼" high x 15½" deep at bottom) accommodates any size trial lens tray; One drawer—20¼" long x 13¾" wide x 3⅛" deep (inside). Back panel is screw-mounted for easy removal.
- Lower part of protective divided lid swings down to provide firm, Formica-topped writing surface. Upper part retracts into cabinet.
- Decorative square panels, both sides, are designed to accommodate H.O.V. All-Purpose Transformers (D) with telephone off-on switch instrument hangers.
- Illumined by 12" fluorescent pencil tube, shielded to prevent glare. Automatically turns on and off by opening or closing top lid.
- May be wall-mounted, set on matching storage cabinet or mounted on attractive legs, with or without casters.
- Lens cabinet (A) when used with storage cabinet (B) fits down into ¼" flange around back and sides which provides safe, non-sliding bond between two pieces.
- Storage cabinet (B) has sliding doors for easy access—and a removable, adjustable shelf. When used as extra cabinet, glass top can be provided.

Catalog No:		
HV 4707	*Lens Cabinet (A) (23" wide x 21¼" high x 15½" deep at bottom) with single drawer—accommodates any size trial lens tray. Lower section of protective lid Formica-topped to use as desk	$115.00
HV 4708	*Storage Cabinet (B) with convenient sliding doors, one removable shelf—flanged to act as firm base for lens cabinet.	$ 80.00
HV 4709	*Set of 4 legs (C) 24" high—with casters	$ 18.00
HV 4710	Glass Top for Storage Cabinet	$ 15.00
HV 2001	All-Purpose Transformer (D)—complete with 2 twist-lock plugs. Black with brushed aluminum face plate	$ 75.00
HV 1805	Coil Cord (Specify instrument to be used).	$ 10.00
HV 7	Spare Bulb	$ 1.25

** Specify grained walnut or light birch finish.*

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Shuron

A paper written by Roy Marks, President of Shuron Optical Company, was presented to the Academy of Optometry in December of last year on the subject of children's eyewear. The paper presented a study which was used by Shuron as the basis for the design of a completely new line of children's frames. These frames, soon to be marketed, are called Pedioptic Frames. The study revealed strong criticisms of present frames for children. Because of the importance of this subject, we are devoting this month's "Shuron Report" to an article by Mr. Marks.

ARE WE DOING ENOUGH for CHILDREN?

The "population explosion" talked about in newspapers, books and magazines is a very real fact in this country. And—as those concerned with the overcrowding of schools, for example, are only too well aware—the "explosion" means a substantial jump in the child population, both in total percentage and in absolute numbers.

Are we, as an industry, doing enough for these children? The answer—surprising and unflattering—is a resounding "No."

You may have read or heard about the recently announced extensive 2-year research programs, carried out by Shuron, on the subject of children's eyewear. This research made it very clear to us that today's frames for children fall deplorably short in the areas of sound design and structure. It furnished us with both motivation and opportunity to take a major step in fulfilling the discovered needs.

When we first decided to bring out a totally new line of children's frames, we were determined to do it on a scientific basis . . . to discover, with modern sampling methods:

1. Whether there was a need for a complete new design concept. 2. Why present frames were inadequate. 3. How they could be improved.

To carry out this part of the study, practitioners and suppliers in 12 major cities were interviewed, and parental attitudes towards children's eyewear were widely sampled at the world-famous Corning Research Center.

This fact emerged: We, as an industry, have done little or nothing—on a factual, scientific basis—to furnish the proper frames for the millions of children who need visual help. True, we're offered many scaled-down versions of adult frames; inverted the pads, taken steps to strengthen bridge and temple areas. But, as shown by the almost overwhelming verdict of both practitioners and parents, children's are still *far* from satisfactory . . . because, in general, they simply *do not fit!*

Report:

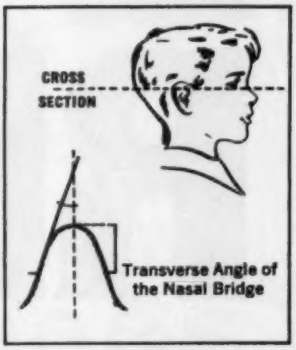
Since a good indication of this became evident very early in our study, we were convinced that something more was needed on which to base our frame designs: Actual anthropometric data on the shape and development of children's faces. We expected to find published research data, with results that we could interpret. Here was the surprise: *No such study* had ever been made! To get this information, we had to do the complete job. For this reason, the study required a full two years of intensive research.

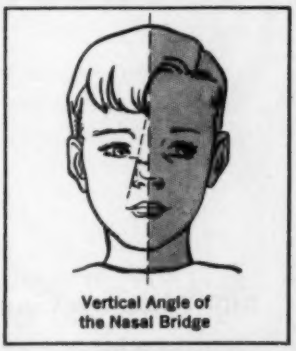
We enlisted, first of all, the skillful cooperation of a renowned anthropologist at Columbia's College of Physicians and Surgeons. His aid was invaluable in setting up the study and in its subsequent completion . . . even to the extent of inventing a new measuring device for the purpose!

As a result of this data-gathering, Shuron now literally possesses the only set of scientific facts on the developmental changes, in two-year age groups, that occur as a result of the growth of the bony structure of the bridge of the nose and the orbital structure surrounding it. It was firmly established that children are *not* miniature adults; that there are definite differences in the bridge area, and that the most significant dimension is the transverse angle of the nasal bridge.

Somewhat surprisingly, the vertical angle of the nose—previously considered the important one—was found to remain practically constant through all periods of growth. Here again, research proved invaluable, in this case showing what is *not* so, even though it was previously acecpted as an obvious and general fact.

The next step was to translate the new data into frames. Shuron design engineers have done so. The new line is appropriately named **Shuron Pedioptic Frames.** The new bridge design, which accurately reflects the changes that occur as the child grows and matures, is called the ***Youthform*** Bridge.





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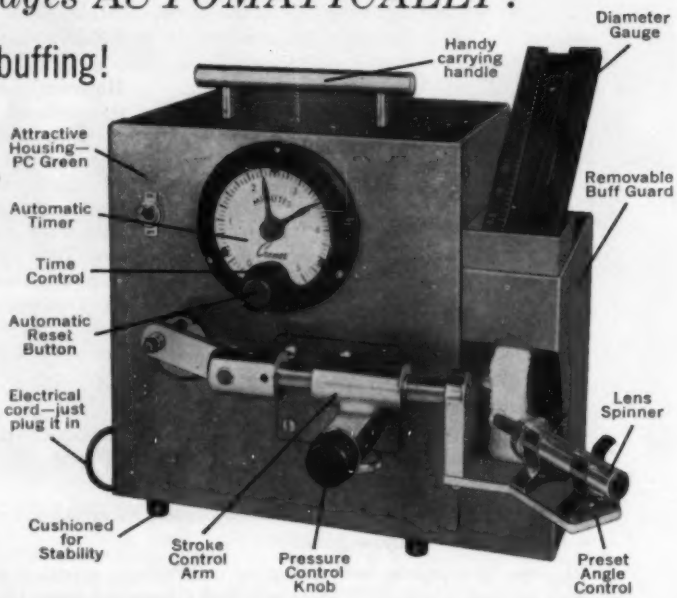

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AMERICAN JOURNAL OF OPHTHALMOLOGY

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UVEITIS SURVEY*

SPONSORED BY THE AMERICAN ACADEMY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

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Baltimore, Maryland

In 1956 the American Academy of Ophthalmology and Otolaryngology applied to the National Institute of Neurological Diseases and Blindness for a grant-in-aid to be used for a "field investigation" of the etiology of uveitis. One of the prime purposes of this project was to supply to American ophthalmologists various antigens used in the etiologic study of uveitis and to make available to them certain laboratory facilities which heretofore had been available in only a few research centers. The background leading to this application was as follows:

For the two preceding decades the study of the etiology of uveitis had been a major investigative project in a number of ophthalmic research institutions—notably the Wilmer Institute, the Proctor Laboratory, the Wills Eye Hospital group, the Ophthalmology Clinic of the University of Iowa, and to a somewhat lesser extent in other ophthalmic centers. As a result of these collected investigations, certain concepts of the etiology of uveitis became crystallized. These may be summarized by saying that in general two main forms of uveitis were recognized. In the early Wilmer studies these were termed *granulomatous* and *nongranulomatous uveitis. Granulomatous uveitis* was believed due to the actual invasion of the uveal tract by the causative pathogen, while *nongranulomatous uveitis* was believed to be a sterile inflammation usually dependent upon a local hypersensitivity to some allergen. In addition, a *mixed type* of uveitis was also recognized. This might present many of the clinical and histologic characteristics of the two main forms. These concepts, the nomenclature adopted, and the clinical characteristics of these various forms of uveitis have been fully described in other communications.[1]

In the search for the exact pathogen causing granulomatous uveitis and for the specific allergen responsible for the hypersensitive state which is the usual basic cause of nongranulomatous uveitis, a number of clinical and laboratory examinations have been employed. By 1953 those various diagnostic procedures had become sufficiently well standardized and adopted to form what is now known as the *Uveitis Survey.* In this survey, a number of antigens and laboratory procedures were used. Many of these were not available, either commercially or on a service basis. As the details of this uveitis survey became publicized, there arose a demand for these antigens and laboratory tests. The research institutions in which these procedures had been developed, and the Public Health Service likewise, were unable to fill these demands.

After various consultations, it appeared that the best way to meet this demand was for a national ophthalmologic organization to sponsor an application to one of the Public Health agencies for a grant-in-aid to finance the preparation and dissemination of diagnostic kits containing a full complement of those antigens and to make available, in some central laboratory, the various labora-

* From the Wilmer Ophthalmological Institute of The Johns Hopkins University and Hosptial.

tory procedures which hitherto had not been available, either to the practicing ophthalmologist or to the nonresearch ophthalmic clinic. It would be the duty of the sponsor to assemble, correlate, and evaluate the results of this field investigation and to make provision for other investigations if deemed proper. The American Academy of Ophthalmology and Otolaryngology undertook this full task. Application for a grant-in-aid was made to the National Institute of Neurological Diseases and Blindness, the grant was duly made, the cultures of organisms from which the bacterial vaccines were prepared were furnished by the Wilmer Institute to a commercial pharmaceutical house, arrangements were made with a designated central laboratory for the performance of the serologic reactions, and the field investigation was launched.

An Advisory Council was then appointed by the Academy to supervise this investigation and to make suggestions for its amplification. As was quite natural in any project of this magnitude, there was some conflict of opinion over the procedures to be followed, and what phases of the project could be best explored. The first decision was to limit the distribution of the kits to established ophthalmic clinics in order that uniformity of examinations might be had. Since these clinics were widely separated geographically, all sections of the country would thus be served, and the epidemiologic as well as the etiologic aspects of uveitis would be covered. A *Brochure of Instruction* on the details and technique of the survey was then prepared by the Council, as well as forms on which the results might be reported. The report forms were later somewhat shortened and amended.

It soon became evident that the field investigation as thus organized did not fully cover the needs of the practicing ophthalmologist not associated with these selected centers. Certain other problems also arose. These latter were due to differences in the technique for certain tests used by the designated central laboratory and those employed by the parent laboratories in which these tests had been developed. These difficulties were finally resolved in the summer of 1960 by the Academy officials, who issued an *Appendix* amending the original *Brochure*. In this change of procedure, the diagnostic kits were made available to any qualified ophthalmologist who would agree to use them as directed and to report the results in the prescribed manner. At the same time the serologic tests were shifted to another laboratory where the technique used and the results of the tests were comparable to those of the various laboratories in which these tests had originally been developed.

The *Uveitis Survey* as now outlined consists of an ophthalmologic examination designed to assemble the basic ophthalmic information and to differentiate, whenever possible, between granulomatous and nongranulomatous uveitis. Thereafter, a number of ancillary examinations are outlined, all designed to determine the precise etiologic factor. These ancillary consultations and special tests outlined in the Academy *Brochure* are certain radiographic examinations, a general physical examination with basic hematologic studies and blood chemistries, otolaryngologic, dental, and urologic consultations searching for systemic foci of infection, sensitivity tests and serologic reactions pertinent to granulomatous uveitis, and other sensitivity tests employed to detect the responsible allergen in nongranulomatous uveitis.

Certain special tests, still largely in the investigative stage, which had been employed in the etiologic study of nongranulomatous uveitis, chiefly in the hope of establishing some laboratory procedures which might be of value in differentiating the two basic types of uveitis, were also suggested for occasional use. The survey now calls for the use of a full battery of routine tests and examinations in all uveitis patients, regardless of the granulomatous or nongranulomatous nature of the uveal inflammation. The principle underlying the use of the full survey in every case is that the results obtained in one type of uveitis

would act as a check or control on those obtained in the other type and thus permit a more exact estimation of the relative value of any specific test.

This survey, as outlined in the Academy *Brochure,* is essentially the one developed in the Wilmer Institute. The earlier reports (1941,[2] 1944,[3] 1953,[4,5] and 1956[6]) dealt usually with particular phases of the diagnostic problem. By 1951, with certain exceptions, the Wilmer survey closely approximated that now outlined in the Academy *Brochure,* and since 1953, the two surveys are basically the same. Therefore, in the Wilmer Institute from 1951 to date, there are the records and the results of essentially the full Academy surveys in the following groups of patients: (a) 101 patients with nongranulomatous uveitis and 107 patients with granulomatous uveitis studied prior to 1953; (b) 97 patients with nongranulomatous and 78 patients with granulomatous uveitis studied from July 1, 1953, to July 1, 1955; and (c) 93 patients with nongranulomatous uveitis and 143 patients with granulomatous uveitis studied from July 1, 1955, to July 1, 1960. Thus there are available for analysis the results of 291 patients with nongranulomatous uveitis and 328 patients with granulomatous uveitis.

As a result of these experiences, certain opinions on the relative value of the particular examinations and procedures recommended, and on the over-all value of the survey, have gradually crystallized. Certain suggestions can also be made whereby the survey might be improved and, in some instances, the time necessary for its completion shortened and the expense to the patients lessened. It therefore appears pertinent at this time to review and to analyze the results already obtained and to report the impressions gained, and the suggestions which appear justified.

I. Differential ophthalmologic diagnosis

Primarily, it may be categorically stated that to date no single test, combination of tests, laboratory procedures, systemic physical abnormalities, alterations in the immunologic reactions or blood chemistries, and so forth, have been found which in themselves are indicative of either granulomatous or nongranulomatous uveitis. The ophthalmologist must therefore depend on the history, the subjective symptomatology, and the objective ocular changes as the only criteria on which the differential diagnosis can be based. These clinical criteria are outlined in the Academy *Brochure,* and the full details have been discussed in other publications, and they need not be repeated here. Suffice to say that in the great majority of cases, a careful history and ophthalmic examination will reveal the true nature of the uveitis. In a few cases, especially those of the mixed type, and the early cases in which the symptomatology has not yet been fully established, the differential diagnosis must be held in abeyance until clarified by further observations.

II. Ancillary consultations

A. Radiographic examinations

The radiographic examinations recommended in the Academy *Brochure* as routine procedures are a chest plate for study of the lung fields and mediastinum, a complete radiographic examination of the teeth for evidences of apical infection, and a routine radiographic study of the accessory nasal sinuses for evidence of active or old infection. The examination of the lung fields and mediastinum is of course related to the search for evidences of systemic granulomatous disease, especially tuberculosis, sarcoidosis, and benign systemic histoplasmosis. The examination of the teeth and nasal sinuses is related to the search for foci of infection. Theoretically, in cases of frank granulomatous uveitis, the dental and sinus films could be omitted; and *vice versa,* in cases of nongranulomatous uveitis, the chest films could be omitted. However, in the over-all picture, the information gleaned by these three examinations is often so important and adds so greatly to the general clinical picture, that it appears worth while to retain these three

routine X-ray examinations in all cases, irrespective of the type of uveitis under study.

B. General physical examination

Since the etiology of uveitis became a subject of special study in the Wilmer Institute, a consultation with a qualified internist has been a routine procedure in practically every case. Over the years it has amply proved its worth. Admittedly, in many cases this consultation has been unrewarding. But in a high percentage of cases it has revealed physical abnormalities which were not before apparent, and in a number of instances has suggested and opened up new avenues for investigation which have finally led to the correct etiologic diagnosis. It is always of value for the following reasons: the second history, taken by the consultant, acts as a check on that taken by the ophthalmologist and occasionally adds important information; an accurate summing up of the general physical condition is of value to the patient and cannot but help the ophthalmologist in his final decision and recommendations; a complete head-to-heels physical examination by a competent internist will often obviate the necessity for other consultations by specialists.

The essential points in the medical consultation are that the internist be interested, and be cognizant of the problems involved in the etiologic study of uveitis, and that the physical examination be complete. It should include the routine examination of the urogenital system, of the throat and accessory nasal sinuses, and of the teeth. It should also include the hemocytology, the basic blood chemistries (blood sugar, urea or nonprotein nitrogen, total serum proteins and the albumin-globulin ratio), and the routine serum tests for syphilis. In the event the consultant has discovered evidences of deep-seated or obscure abnormalities, the medical examination should be expanded to include the tests necessary to clarify the diagnosis, that is, additional blood chemistries, further blood studies, tests for renal and liver function, a gastro-intestinal series, and so forth.

It is therefore recommended that the medical consultation be continued as an integral part of the survey, regardless of the type of the uveitis under study.

C. Examination for foci of infection

In the 1956 Wilmer Institute report, the incidence of systemic foci of infection in 187 patients with nongranulomatous uveitis and 185 patients with granulomatous uveitis was given. To these cases can now be added the 93 patients with nongranulomatous uveitis and the 143 with granulomatous uveitis who were surveyed in the 1955-1960 period. As a result, there is now information on the occurrence of systemic foci of infection in 280 patients with nongranulomatous uveitis, and in 328 patients with the granulomatous form of the disease. This information is given in Table 1.

The uveitis cases studied in the 1955-1960 period give information relative to the locus of the infected foci in patients with either nongranulomatous or granulomatous uveitis. This additional information is given in Table 2.

From these two tables it is evident that systemic foci of infection are twice as frequent in patients with nongranulomatous uveitis as in those with granulomatous uveitis. Such focal infections are most frequent in the upper respiratory tract, the accessory nasal sinuses, and the tonsils, with the teeth and genito-urinary tracts being involved in descending order of importance. It is also of particular interest that in 40 of the total of 280 patients with nongranulomatous uveitis,

TABLE 1

Incidence of systemic foci of infection in patients with granulomatous and nongranulomatous uveitis (1951–1960)

Type of Uveitis	No. of Cases	Foci of Infection Found	
		Number	Percentage
Granulomatous	328	88	27
Nongranulomatous	280	153	55

TABLE 2

LOCUS AND INCIDENCE OF FOCAL INFECTIONS IN PATIENTS WITH GRANULOMATOUS AND NONGRANULOMATOUS UVEITIS
(including multiple foci)

Type of Uveitis	No. of Cases	Sinus-Tonsil Infections		Dental Infections		Genito-urinary Infections		Over-all Total	
		No.	Per-cent	No.	Per-cent	No.	Per-cent	No.	Per-cent
Granulomatous	143	23	15	6	4	4	3.0	33	23
Nongranulomatous	93	52	34	14	15	7	7.5	53	57

the patients were proven hypersensitive to organisms cultured from their own foci of infection.

D. OTHER ANCILLARY CONSULTATIONS

Our impressions of the value of otolaryngologic, dental, and urologic or gynecologic consultations in a survey for the etiology of nongranulomatous and granulomatous uveitis may be summarized as follows:

Otolaryngologic consultation. In nongranulomatous uveitis, if the patient gives a history of previous sinus, pharyngeal, or tonsillar infection, if the examination by the internist reveals any evidence of such infection, or the radiographic examination shows clouding or a fluid level in the accessory nasal sinuses, then consultation with an otolaryngologist is imperative. This consultation should include cultures of the infected sinuses, tonsils, or adenoid tissues, and the preparation of autogenous vaccines from any Streptococci, Pseudomonas or other organisms of suspected importance isolated therefrom. If there is no history suggestive of a previous otolaryngologic infection, if the examination by the internist has disclosed no evidence of such infection, and if the X-ray pictures of the sinuses are clear, the otolaryngologic consultation may be omitted.

In frank, uncomplicated, granulomatous uveitis, the otolaryngologic consultation may be safely omitted, except in cases in which the infection is so manifest it requires attention for its own sake.

Dental consultation. In nongranulomatous uveitis, if the dental X-ray films have shown any evidence of apical infection, then consultation with an oral surgeon is indicated. The infected tooth or teeth should be extracted and a culture made from the socket in all cases except the occasional ones in which such cultures can be obtained without loss of the tooth. Autogenous vaccines should be prepared from any Streptococci, Pseudomonas, or other pathogenic organisms so isolated, and the patient tested for hypersensitivity to these. If the X-ray films of the teeth are negative, the dental consultation may be omitted.

This examination may safely be omitted in all cases of frank granulomatous uveitis, except in those in which the dental films have revealed an infection of such degree that it requires treatment for the general hygienic treatment of the patient.

Urologic-gynecologic consultations. A urologic or gynecologic consultation on all uveitis patients has been routine in the Wilmer Institute since the investigations on the etiology of uveitis were first undertaken. In the over-all picture these consultations have only occasionally been rewarding. Our experiences may be summarized as follows:

In two patients with granulomatous uveitis, the urologic consultation has disclosed a tuberculous epididymitis which pointed the way to a correct etiologic diagnosis. In three patients with nongranulomatous uveitis, a diagnosis of Reiter's syndrome was entertained, but in two of these it was discarded, the actual condition apparently being a burned-out gonorrhea with a secondary infection. In 228 male patients with nongranu-

lomatous uveitis, seen between 1951 and 1960, there were 27 cases of active chronic prostatitis, an incidence of 12 percent. In six of these the prostatitis was apparently related to the uveitis, for the patients gave positive reactions to streptococci isolated from their prostatic secretion. It is also interesting that three of these six patients were negative to all the streptococcal vaccines in the diagnostic kit.

These figures are in sharp contrast to those recently reported from England by Catterall.[7] In 105 patients with acute uveitis, this investigator found a 33-percent incidence of Reiter's syndrome and an 88-percent incidence of chronic prostatitis. However, our figures appear to be in accord with figures from American urological clinics. For example, in the last 14 years, there are only 13 cases of Reiter's syndrome listed in the diagnostic file of the Brady Urological Clinic, while in this same time there are approximately 4,700 cases of chronic prostatitis.[8] The only explanation for the discrepancy between the English and American figures is that either Reiter's disease is a rarity in America, or that different diagnostic criteria for this syndrome are employed on the two sides of the Atlantic.

The gynecologic examination has been equally unrewarding. In two patients this examination revealed a tuberculous focus in the pelvic organs, and in two the finding of cystic ovaries helped point the way to a final diagnosis of brucellosis as the etiologic factor. In several cases of nongranulomatous uveitis, the finding of chronic inflammatory pelvic disease suggested a relationship between the infection and the uveitis, but in no case was this suspicion confirmed by the demonstration of a specific hypersensitivity to autogenous organisms. In several cases the examination revealed evidences of an early malignancy, but this was obviously unrelated to the uveitis.

In view of this paucity of significant results, the value of routine urologic or gynecologic examinations appears somewhat doubtful. In both granulomatous and nongranulomatous uveitis, these examinations may well be restricted to patients in whom the history or general physical examination has suggested the presence of a urogenital or pelvic infection. Failing such suggestive evidence, it is probable that special consultations with either a gynecologist or a urologist could be omitted from the survey with but small danger of great loss.

III. Immunologic reactions in granulomatous uveitis

A. Sensitivity tests

The antigens provided in the Academy diagnostic kit for the etiologic diagnosis of granulomatous uveitis are PPD (purified protein derivative) for the detection of hypersensitivity to tuberculin, toxoplasmin, brucellergen, and three fungus antigens—blastomycin, coccidioidin and histoplasmin. Our experience with these antigens may be summarized as follows:

Tuberculin hypersensitivity. Since the Wilmer Institute was founded in 1925, it has been the custom to test all patients, studied for the etiology of uveitis, with graduated amounts of old tuberculin (OT) —Mantoux test. However, in many of the patients studied before 1953, the differentiation between granulomatous and nongranulomatous uveitis was not sufficiently sharp to permit any valid conclusions on the relative incidences of tuberculin hypersensitivity in these two forms of uveitis. We have, therefore, restricted the analysis of the tuberculin hypersensitivity to those patients seen since 1953. In this analysis, patients who had previously received tuberculin desensitization therapy were excluded.

The results of this analysis are shown in Table 3. In this table, the cases of granulomatous uveitis are reported under two classifications: (a) cases in which the final diagnosis was tuberculous uveitis and (b) cases in which the final diagnosis was some etiologic factor other than tuberculosis, or was undeterminable.

TABLE 3

TUBERCULIN HYPERSENSITIVITY IN DIFFERENT TYPES OF UVEITIS

Type of Uveitis	No. of Cases	High Sensitivity		Moderate Sensitivity		Low Sensitivity		Anergy	
		No.	Percent	No.	Percent	No.	Percent	No.	Percent
Granulomatous (tuberculous)	47	31	66	11	23	3	7	2	4
Granulomatous (other than tbc.)	178	17	10	24	13	52	29	85	48
Nongranulomatous	163	13	8	18	11	37	23	95	58

In this table, "high sensitivity" indicates a positive reaction to 0.001 mg. of old tuberculin or the first strength of PPD; "moderate sensitivity" indicates a negative reaction to 0.001 mg. of old tuberculin or the first strength of PPD, but positive reactions to 0.01 mg. of old tuberculin or the intermediate strength of PPD; "low sensitivity" indicates negative reactions to 0.001 and 0.01 mg. of old tuberculin or the first and intermediate strengths of PPD, while there was a positive reaction to 0.1 mg. of old tuberculin or to the second strength only of PPD. "Anergy" indicates negative reactions to all three dilutions of old tuberculin or to the three strengths of PPD.

These findings clearly demonstrate the high incidence of an undue tuberculin sensitivity and the low incidence of tuberculin anergy in the tuberculous form of granulomatous uveitis, and the exact reverse in the nontuberculous form of granulomatous uveitis and in nongranulomatous uveitis. They likewise show the value of the tuberculin test. While it is well recognized that the demonstration of a high degree of tuberculin hypersensitivity is not in itself diagnostic of a tuberculous etiology for the uveitis, and that a negative test does not exclude tuberculosis, nevertheless the finding of a marked hypersensitivity to either old tuberculin or to PPD immediately focuses attention on the probability of a tuberculous etiology, the finding of anergy argues against such an etiology.

The tuberculin test is certainly one of the corner stones in the always somewhat tentative diagnosis of tuberculous uveitis. It is highly suggestive and is one of the links in the chain of evidence which support a final etiologic diagnosis of tuberculosis. The tuberculin sensitivity should certainly be determined in every case of uveitis as an integral part of the etiologic study.

Toxoplasmin. A toxoplasmin skin test is indicated in every case of granulomatous uveitis. Acquired toxoplasmosis is a widely disseminated disease, and the skin test may remain positive long after the disease is inactive and the dye test has faded. A negative test does not exclude the possibility of a recently acquired toxoplasmosis. In our experience,[9] the skin test with toxoplasmin may be negative in the early stages of an active acquired toxoplasmic uveitis, and later become positive as the disease progresses. Therefore, in an early uveitis, in which toxoplasmosis is suspected, if the first skin test is negative, it should be repeated after a lapse of two to three weeks. A late developing positive skin test, together with a rising dye test, and at times a developing complement-fixation reaction, is pathognomonic of a recently acquired toxoplasmic infection. In our experience, in patients with a granulomatous uveitis and a positive toxoplasmin skin test, the dye test was positive in minimum titers of 1:64, 1:32, and 1:16, respectively, in 85, 90, and 95 percent of the cases. Its value as a screening test is therefore obvious. It is an essential test in all uveitis cases.

Brucellergen. A brucella uveitis occurs only in the chronic phases of the disease, when the skin test with either brucellergen or brucellin is usually positive. However, the

skin test may remain positive for months or years after a patient has fully recovered from an attack of acute brucellosis, and the positive skin test is only an indication that at one time the patient had the disease. Further, its persistence in the chronic disease is somewhat unpredictable—occasionally patients with almost undoubted brucella uveitis, with clinical and other serologic evidence of a chronic infection, will have negative skin reactions with both antigens. A positive skin test, therefore, is only one of the tenuous links of evidence which may lead to an ultimate presumptive diagnosis. When positive, it immediately directs attention to the possibility of brucellosis as the etiologic factor. Although not of great importance, it should be done in every case of granulomatous uveitis. This is especially true in the early attacks of a brucella iridocyclitis, when the differential diagnosis between granulomatous and nongranulomatous uveitis may be exceedingly difficult.

Fungus antigens. Blastomycin, coccidiodin, and histoplasmin are the three fungus antigens supplied in the Academy diagnostic kit. The early investigations on hypersensitivity to histoplasmin showed that occasional cross reactions to blastomycin and coccidiodin were sometimes observed both in patients and animals with benign systemic histoplasmosis. However, with the purified antigens now available and supplied in the diagnostic kit, we have observed no cross reactions between these antigens, and this appears to be a negligible factor. In 112 patients tested with all three of these antigens, we have yet to observe a single positive reaction to either blastomycin or coccidioidin. While both coccidioidomycosis and blastomycosis are proven causes of an occasional case of granulomatous uveitis, and tests for hypersensitivity to these antigens should be continued, they must be considered very rare and relatively unimportant factors. Benign systemic histoplasmosis, however, is in a quite different category.

Benign histoplasmosis is a relative newcomer among the etiologic factors to be considered in the study of granulomatous uveitis. Histoplasmin was first used occasionally in the Wilmer Institute beginning in 1948, and only in recent years, when it became commercially available, has it been used as routine in the uveitis survey. Our full experiences with this antigen have recently been reported.[10] (Table 7 with footnote.) Suffice to say here that it has been used in the full surveys of 186 patients with granulomatous uveitis and in 107 patients with nongranulomatous uveitis. In the group of patients with granulomatous uveitis the test was strongly positive in 62 instances, an incidence of 33 percent. In the nongranulomatous group it was positive in 16 patients, an incidence of 15 percent. Collateral evidence and the exclusion of other etiologic factors established the probable etiologic diagnosis of benign systemic histoplasmosis in 19 or 10 percent of the positive reactors in the granulomatous group, and suggested this possibility in one of the patients with nongranulomatous uveitis.

Benign systemic histoplasmosis is an extremely wide-spread infection, especially in certain localities, and the *Histoplasma capsulatum* is a notorious sensitizer. Thus, while a violently positive reaction to histoplasmin in a patient with granulomatous uveitis does not establish an etiologic diagnosis of histoplasmosis, a negative reaction to histoplasmin does exclude this possibility. Intracutaneous tests with this antigen should therefore be continued in every case of granulomatous uveitis, and, if only for investigative purposes, in all cases of nongranulomatous uveitis.

Uveal pigment. This antigen is used only in cases of suspected sympathetic ophthalmia, and even here it is of limited value. The pigment is slowly absorbed, and positive reactions are difficult to detect clinically. The injected skin must be excised after two weeks and examined histologically for clumping of the pigment in a negative test, and for epithelioid cell infiltration and pigment phagocytosis which are the criteria of a positive reac-

tion. While patients with sympathetic ophthalmia almost invariably give positive skin tests with pigment at some phase of the disease, usually the early stages, the persistence of the hypersensitivity is unpredictable, and the test is now used only to confirm a clinical diagnosis.

Lens protein. This antigen test is used only in cases of suspected lens-induced uveitis. It is invariably positive in cases of active endophthalmitis phacoanaphylactica and, in our experience, also in cases of the so-called phacotoxic uveitis, apparently the only difference being in the intensity of the reaction. When the uveitis subsides, the test tends to become weaker, although it may persist for years. The test is of value only when the clinical picture suggests a len-induced uveitis.

Serologic reactions

A. Specific anti-Treponemal tests

The routine serum tests for syphilis are dependent upon a substance known as the "Wassermann reagin." This reagin occurs in the blood plasma in increased amounts in active syphilis, but tends to disappear after antisyphilitic treatment, and also in latent syphilis. It also occurs in increased amounts in certain nonsyphilitic diseases, notably some of the collagen diseases, and is responsible for what are called "biologic false positives" of the Wassermann reaction. In order to detect specific antitreponemal antibodies in latent syphilis, and to avoid the confusion caused by biologic false positives, certain specific tests with treponemal antigens have been devised. These are the treponemal immobolization test, the Treponema pallidum adherence test, the fluorescein antibody test, and complement-fixation tests with various treponemal antigens. These tests all have, to a greater or lesser degree, the advantages that they remain positive long after the Wassermann reagin has disappeared from the blood, are unaffected by prolonged antisyphilitic treatment, and avoid biologic false positive reactions. The most readily available of these tests is the Reiter complement-fixation reaction. The antigen is prepared from a sacrophytic Treponema which can easily be cultivated on artificial media, is available commercially, presents few if any technical difficulties, and the test can be performed in any Wassermann laboratory.

The uveitis of latent syphilis tends to occur in the late stages of the infection, when the Wassermann test may be negative. Therefore, in a patient in whom the routine tests for syphilis are negative, yet in whom there is still a lurking suspicion of syphilis, these tests for complement-fixing antibodies specific for Treponema may suddenly clarify and establish the diagnosis.

Our experience in the Wilmer Institute has been chiefly with the treponemal immobilization test. This test, however, is extremely difficult technically, and is highly expensive. It has now been largely supplanted by the Reiter complement-fixation test. Our limited experience with this latter test indicates that in the uveitis of late syphilis, it is an adequate substitute. It is, therefore, recommended that, in cases in which the routine tests for syphilis are negative but in which the possibility of a syphilitic etiology still persists, and also in cases in which there is a suspicion that a reported Wassermann reaction may be a biologic false positive, arrangements be made to have Reiter's complement-fixation test run on the patient's serum.

B. The Sabin-Feldman dye test for toxoplasmosis

This test has become the standard test on which a diagnosis of ocular toxoplasmosis is based. It is dependent upon specific toxoplasmic antibodies, which in the presence of an accessory factor in normal serum, inhibit the staining of the toxoplasma parasite with methylene blue. Heretofore, in the various laboratories which have used this test as an investigative procedure, there has been a remarkable conformity in the results obtained. The test becomes positive in

the early stages of the infection, rapidly increases in titer as the infection progresses, and may remain positive in decreasing titer for seven years or longer after all symptoms have subsided.

In our experience in the Wilmer Institute, in every case of active, granulomatous uveitis in which the final etiologic diagnosis was toxoplasmosis, there has been a minimum dye test titer of 1:64. In some acute, progressive cases, the titer may reach such astronomic heights as 1:16,384 plus! These results and titers have been duplicated and confirmed on repeat tests in the same laboratory (National Institute of Microbiology —Dr. Leon Jacobs). A minimum titer of 1:64 has therefore been adopted as the dye test criterion for a positive diagnosis of toxoplasmosis in a case of active uveitis, although in inactive or burned-out cases, the titer may be much lower.

The Sabin-Feldman dye test is at present the basic test in the diagnosis of a toxoplasmic uveitis. Since toxoplasmosis is probably the most important cause of adult granulomatous uveitis, it is essential that it be done in every case.

C. The hemagglutination reaction for toxoplasmosis

The hemagglutination test is based on the ability of some antiserums to agglutinate specifically sensitized cells. It was employed by Middlebrook and Dubos for the serologic diagnosis of tuberculosis, and when used for this purpose is known as the Middlebrook-Dubos reaction. It has recently been modified and adapted by Jacobs and Lunde[11,12] for the serologic diagnosis of toxoplasmosis. It has not as yet been used to any extent as a routine diagnostic procedure, and we have had no experience with it. Dr. Jacobs,* however, has run parallel tests with this hemagglutination reaction and with the Sabin-Feldman dye test on a series of serums of patients with uveitis in the Wilmer Institute, and reports an accurate correlation between the two diagnostic procedures. This test presents few technical difficulties, and is well within the range of any well-equipped diagnostic laboratory. It may well prove to be an adequate substitute for the dye test. Further investigation will be needed to establish this.

D. The agglutination reaction for leptospirosis

Barring the actual isolation of the parasite, the agglutination-lysis reaction is the most sensitive and reliable test for leptospirosis. However, it requires antigens of several strains of the living parasite, and is therefore unavailable in the usual service laboratory. The test provided for in the field investigation is the straight agglutination reaction, which is done with stock antigen composed of dead organisms of the required strains.

Our experience with this test is limited to a few patients in whom a history of a possible hepatic infection or jaundice has aroused the suspicion of a previous Leptospira infection. We have yet to record a single positive result, or to observe a case of uveitis which could logically be attributed to leptospirosis. While leptospirosis is undoubtedly a proven cause of an occasional case of uveitis, it is obviously an extremely rare one. With danger of but small loss, it could be omitted from consideration in the usual routine survey, and employed only in the occasional case where there is a history suggestive of a possible prior Leptospira infection.

E. The agglutination test for brucellosis

Our experience with this test may be summarized as follows:

The test was done on the serums of 176 of the 200 cases reported in 1944.[3] Since then, with few exceptions, it has been done routinely in every case of uveitis surveyed in the Wilmer Institute. Up to 1952, the agglutination test was done against antigens of living organisms. Since that date, stock

* Personal communication.

antigens of dead organisms have been used. Undoubtedly, the test with living organisms is more sensitive, and the titers obtained are somewhat higher than those with the dead, stock antigens. The difference, however, does not compensate for the great danger entailed in keeping living brucella organisms in a diagnostic laboratory, and preparing antigens from them.

In the 15 cases of brucella uveitis reported in 1944, two patients gave negative tests, and the remaining 13 gave titers varying from 1:20 to 1:320. In the 21 cases seen between 1950 and 1960, in which the diagnosis of a brucella uveitis appeared justified, this same pattern of low agglutination titers was observed. Similar low titers have been observed in medical patients who did not have uveitis but who were believed to have chronic brucellosis. In the few patients we have examined and who were known to have had acute brucellosis but had apparently made a complete recovery, the agglutination titers varied from zero to rarely more than 1:40. In short, patients who have recovered completely from an acute infection sometimes show low agglutination titers as evidence of their former disease. While these titers were generally lower than those observed in patients who developed the chronic form of the disease, the difference is not great. At best, a positive agglutination reaction in chronic brucellosis is only one of the links of tenuous evidence on which the final diagnosis must be made. On account of the somewhat variable picture of brucella uveitis, it is recommended that an agglutination test be done in every case surveyed, but that the result be interpreted in the light of the history, and other clinical and laboratory findings.

F. Complement-fixation reactions in granulomatous uveitis

Our experience with the complement-fixation reaction as a diagnostic procedure in granulomatous uveitis, other than that due to syphilis, may be summarized as follows:

Brucellosis. In the 1944 report, complement-fixation reactions against a brucella antigen were done in 76 patients. In 21 of these the reaction was positive. However, 18 of these 21 serums also gave positive reactions against antigens of gonococci or other gram-negative organisms. On account of this extremely high incidence of cross-reactions and probable false positives, the test was abandoned.

Toxoplasmosis. In 1956, we reported the results of complement-fixation tests against a toxoplasma antigen in 92 cases of uveitis. In 30 cases of nongranulomatous uveitis the test was negative in all. In 62 cases of granulomatuos uveitis, 38 patients gave positive skin and dye tests for toxoplasmosis, and it was believed this was the correct etiologic diagnosis. However, in these 38 patients, the complement-fixation reaction was positive in only seven instances!

It was concluded that the test was of little value, that the reaction was irregular in its appearance, and that the complement-fixating antibodies tended to disappear early. Only when a positive complement-fixation reaction develops in the course of an acute infection and increases in titer as the infection progresses, does the test appear to be of any diagnostic value. It was therefore recommended that it be abandoned as a routine diagnostic procedure.

Histoplasmosis. Extensive studies in other clinics have shown that, while complement-fixing antibodies develop early in benign systemic histoplasmosis, they tend to disappear while the histoplasmin skin test becomes strongly positive. Since the central, serous lesions in the fundus, which direct the patient to the ophthalmologist, appear late in the course of the benign systemic infection, one would not expect to find a consistently positive complement-fixation reaction in these ocular cases.

This has been exactly our experience. In the cases of histoplasmic chorioretinitis reported from the Wilmer Institute in 1959, and in those since observed, only very occasionally was the complement-fixation re-

action for histoplasmosis positive and then only in very low titers, 1:4, 1:8, and never over 1:16. All of these cases showed violent hypersensitivity to histoplasmin, spotty pulmonary calcification, and usually anergy to tuberculin. It was therefore concluded that a negative complement-fixation reaction was of no significance, and the occasional low titer positive reaction was only confirmatory evidence. It is therefore recommended that the complement-fixation be done only as an investigative procedure to gather further data, and that it be abandoned as a routine diagnostic test in the uveitis survey.

IV. Sensitivity studies employed in the etiologic study of nongranulomatous uveitis

A. Stock bacterial vaccines

The Academy diagnostic kit contains 10 antigenically distinct strains of alpha streptococci, 42 antigenically distinct strains of the subgroup A of the Beta streptococci (Lancefield classification), representatives of the B, C, D, F, and G subgroups, and a gamma strain. It also contains a gonococcal antigen, which is now chiefly of academic interest only. Our experience with these stock streptococcal vaccines prior to 1955 has already been reported.[6] The results of the 1956 study, combined with the 93 cases of nongranulomatous uveitis and 126 cases of granulomatous uveitis studied since 1955 (in all of which examinations for bacterial sensitivity were made), give our total experiences with the Academy kit antigens in 602 cases of the two main types of uveitis. These are shown in Table 4.

The important points shown in Table 4 are the high incidence (76 percent) of hypersensitivity to these streptococcal antigens shown by patients with nongranulomatous uveitis and the lower, but significant, incidence of hypersensitivity shown by the two control groups. These figures of 22 and 30 percent positive reactors in the two control groups at once arouse the suspicion that

TABLE 4

Incidence of hypersensitivity to stock streptococcal vaccines in patients with nongranulomatous uveitis and in controls

Type of Patient	No. of Cases	Positive Reactors to Stock Vaccines
Nongranulomatous uveitis	291	218 (76%)
Granulomatous uveitis	311*	93 (30%)
Non-uveitis patients	100	22 (22%)

* Tests for bacterial sensitivity were not done in 17 of the 328 patients with granulomatous uveitis.

the 76 percent of positive reactors in the nongranulomatous group include an appreciable number of patients in whom the demonstrated hypersensitivity might be unrelated to the uveitis. This suspicion is confirmed by the fact that in the specific desensitization studies[6] there was an appreciable (22 percent) failure rate. When these factors (the failure to demonstrate a specific hypersensitivity and the failure rate in specific desensitization) are considered from the statistical standpoint, the success rate in the demonstration of the responsible allergen with the stock vaccines in the diagnostic kit and the confirmation of such responsibility by successful specific desensitization fails to approximately 60 percent.

Several other points were noted in these hypersensitivity studies with the stock streptococcal vaccines, one of which is of high importance. These are as follows:

The studies reported in 1953 and in 1956 were all done with vaccines prepared in the bacteriologic laboratory of the Wilmer Institute. The alpha vaccines were all prepared from alpha streptococci isolated from foci of infection in patients with nongranulomatous uveitis, and to which these patients had been proven highly sensitive. When the various strains of streptococci were turned over to the commercial laboratory which prepared the final vaccines for the diagnostic kits, it was found that the stored frozen alpha strains from which the original Wilmer vaccines had been prepared were, almost without exception,

completely dead. It was therefore necessary to provide other alpha strains from those at hand and select from them 10 new antigenically distinct strains. This was accordingly done. However, these were not strains isolated from patients with nongranulomatous uveitis and which had been proven sensitizers related to a uveitis. In the cases studied from 1957 to 1960, these new alpha vaccines in the diagnostic kit were used, and not a single positive reaction to them has been observed. In our experience, it appears that these alpha strains in the present diagnostic kit are quite worthless. It is recommended that when alpha streptococci are isolated from foci of infection in a patient with nongranulomatous uveitis, and the patient is proven sensitive to his autogenous organism, that cultures of such be sent to some central laboratory for further investigation, with the idea of thus assembling a new series of alpha strains for incorporation in the diagnostic kit, in substitution for the apparently worthless alpha vaccines now therein.

The second point of possible interest is the decrease in the incidence of positive reactions to the subgroup A of the beta streptococci from 80 percent in patients tested with the old Wilmer vaccines to 67 percent positive reactions obtained with those in the diagnostic kit. This may not be of importance, but it has been our distinct impression that while the positive reactions with these new vaccines parallel those observed with the original Wilmer vaccines, they are somewhat less intense. Thus, in borderline cases, more attention should be paid to single plus reactions.

One further point should be noted. When the study with Lancefield subgroup A was first begun, there were available only the 42 strains now in the diagnostic kit. Since that time Dr. Lancefield has isolated five additional antigenically distinct strains which belong in this subgroup. It is suggested that these strains be obtained, that test vaccines from them be prepared and these be added to the present diagnostic kit. It is quite possible that by this simple procedure, the success rate for the demonstration of the responsible bacterial allergen might be further increased.

B. Autogenous bacterial vaccines

The Academy *Brochure* stresses the importance of determining the bacterial flora of any autogenous focus of infection in the patient, the preparation of test vaccines from any suspected organisms, and testing the patient for hypersensitivity to such bacteria. The importance of this cannot be overemphasized.

In our experience to date[1] in patients with nongranulomatous uveitis, 68 such vaccines have been prepared, and the patient tested for hypersensitivity to them. In 40 instances, these tests were positive, often intensely so. It is especially noteworthy that 15 of these positive reactors to their own autogenous streptococci were completely negative to all the stock streptococcal vaccines in the diagnostic kit, and that all of these patients did conspicuously well on desensitization with their own autogenous organisms. Had this possibility not been considered, this therapeutic procedure would have been missed. When these 15 patients are added to the 218 positive reactors to the stock vaccines, the overall incidence of a demonstrated bacterial hypersensitivity in the 291 patients with nongranulomatous uveitis rises to 80 percent and, after making allowances for possible unrelated sensitivities, the success rate for the demonstration of a bacterial hypersensitivity related to the nongranulomatous uveitis is increased statistically to 64 percent.

Parenthetically, it may be stated here that all efforts to shorten or abridge the labor of these bacterial sensitivity tests has been unavailing. Our failure with composite master mixtures of 10 to 12 strains has already been reported. More recently we have reviewed the histories of the positive reactors, hoping to find some strains of the subgroup A of the betas which had given uniformly negative reactions and which therefore could be omitted. This effort was also unsuccessful.

While numbers 11, 40, and 41 were the strains most frequently incriminated, there was no single strain which was uniformly negative.

Similarly, there appears to be no way in which the labor of determining the bacterial flora of autogenous foci of infection, and the preparation of test vaccines can be abridged. In our limited experience, the "pathogen selective" technique advocated by Harley[13] is equally laborious and has been ineffective in the isolation of strains which uniformly give positive reactions. There appears to be no alternative to the procedure recommended in the Academy *Brochure*.

C. Nonbacterial antigens

A quiet, low-grade, nongranulomatous iritis is a frequent, or even a constant, complication of systemic serum sickness. Serum sickness is now something of a rarity and when it occurs, offers no diagnostic problem. Similarly, nongranulomatous iritis is sometimes observed in drug hypersensitivity. The portal of entry is usually by absorption through the cornea, and the presence of the concomitant dermatitis and conjunctivitis after instillation of the offending drug immediately reveals the nature of the allergen. The occasional iridocyclitis which may follow the oral ingestion of a drug to which the patient is hypersensitive may be more puzzling. However, the accompanying systemic symptoms indicate the etiologic factor, and there is rarely any diagnostic difficulty.

There are several almost convincing reports in the literature of cases of nongranulomatous iridocyclitis apparently due to hypersensitivity to foods or air-borne allergens. We have encountered several cases in which the patient associates the attacks with the ingestion of certain foods, exposure to pollens, animal dander, and so forth, and one case in which the patient was certain the iridocyclitis followed insect bites. In none of these cases have extensive allergy studies revealed any sensitivity which could logically be associated with the iritis. The only recommendation which we can make is that, when such cases are encountered, the patient be referred to a competent allergist for study, but in our experience such studies have been negative.

D. Hypersensitivity to viral agents

There is conclusive evidence that a nongranulomatous iridocyclitis is frequently associated with certain mild systemic viral infections. The usual failure to isolate the virus from the intraocular fluids has led to the supposition that this iritis is due either to the antigenic or toxic properties of the virus. While this is probably true, it is as yet unproven. It is also possible that symbiotic viruses may be the responsible allergen, but again there is no proof of this, and there is no readily available method of testing for such hypersensitivity. While we concur in the view that viral or rickettsial agents may ultimately prove to be of high importance in the etiology of uveitis, the problem up to this time has been an almost completely baffling one. Our experience in this field is so limited, we have no recommendations to make.

V. Examinations occasionally employed in the etiologic diagnosis of endogenous uveitis

During the 1955-1960 period, various special tests and examinations have been run on a limited number of uveitis patients in the hope that such investigations might (a) reveal some change in the blood chemistries or some immunologic reaction which might be indicative of one or the other type of uveitis, or (b) that it might open up new avenues for further investigation in the problem of the etiology of uveitis. The tests and examinations thus explored are certain blood chemistries, the antistreptolysin-O titer, the Rose-Heller test, buffy coat smears for lupus cells, the cephalin flocculation test, the thymol turbidity index, and the C-reactive

protein titer of the blood serum. For what it may be worth, our limited experience may be summarized as follows:

A. Blood uric acid

In our over-all experience with uveitis during the last three decades, we have observed only one case of uveitis associated with gout, and in this case there were other etiologic factors to which the uveitis could be attributed. There is one case in the Proctor Laboratory series in which an associated gout was the only positive finding. When we first began to use the Academy kit, we dutifully ran blood uric acid determinations in several hundred cases. The results were all consistently negative. Since gout is now something of a rarity, and appears to be one of the most highly doubtful etiologies ever suggested for uveitis, we have abandoned these blood uric acid determinations as a useless procedure.

B. Electrophoretic pattern

Paper electrophoretic studies of the blood serum proteins have been done on 69 patients with nongranulomatous uveitis and on 61 patients with granulomatous uveitis. The results of these studies are summarized in Table 5.

The possibly significant findings in Table 5 are: (a) the wide variation in the alpha and beta globulins in the nongranulomatous cases compared to their relative stability in the patients with granulomatous uveitis; (b) the 42-percent increase in the alpha globulins in nongranulomatous uveitis cases; (c) the marked decrease in the gamma globulin in both groups—42 percent in the nongranulomatous cases and 51 percent in the granulomatous ones. There is no immediate explanation for the instability of the alpha and beta globulin fractions or for the relative increase in the alpha globulins in the patients with nongranulomatous uveitis. The marked decrease in the gamma globulins in both groups suggests a decrease in the circulating antibodies, which are known to be contained in the gamma globulin. In both granulomatous and nongranulomatous uveitis there is a high degree of tissue hypersensitivity—in nongranulomatous uveitis to bacterial antigens and in granulomatous uveitis to the specific protein of the pathogen invading the uvea. This apparent decrease in the circulating antibodies in both conditions might be construed as an argument for the view held by many immunologists that tissue hypersensitivity, or increased vulnerability to antigenic assault, is largely due to lack of a protective screen of antibodies in the blood plasma. This, however, is little more than idle speculation.

There are no recommendations to make. Obviously, from this study, a determination of the electrophoretic pattern of the blood serum, even as a screening test, is quite worthless in the etiologic diagnosis of the individual case of either granulomatous or nongranulomatous uveitis.

TABLE 5

Results of electrophoretic studies of the blood serum in patients with granulomatous and nongranulomatous uveitis

Type of Uveitis No. of Patients	No. and Percent		Abnormalities Disclosed—No. and Percent							
	Normal	Abnormal	Albumen		Alpha Glob.		Beta Glob.		Gamma Glob.	
			Inc.*	Dec.†	Inc.	Dec.	Inc.	Dec.	Inc.	Dec.
Granulomatous	15	46	6	7	8	13	7	8	7	31
61 cases	25%	75%	10%	11%	13%	21%	11%	13%	11%	51%
Nongranulomatous	23	66	7	7	29	18	20	16	8	29
69 cases	33%	67%	10%	10%	42%	26%	29%	23%	12%	42%

* Increased † Decreased

C. Other blood chemistries

The value of determinations of the total serum proteins and of the albumin-globulin ratio in sarcoidosis is well recognized, and is borne out in our experience. Numerous determinations of other blood fractions—calcium, phosphorus, lipids, and so forth—have been made during the Wilmer Institute investigations. Valuable as these are in the diagnosis of various associated medical conditions, they have been without value in the etiologic diagnosis of uveitis.

D. Antistreptolysin-O titers

The antistreptolysin-O titer of the blood serum is known to increase in varying degree after certain streptococcal infections. How long the increased titer persists after different types of infection is not clearly known. Since there is reason to believe nongranulomatous uveitis is frequently associated with an immunologic change resulting from a prior streptococcal infection, this titer was determined in a limited number of nongranulomatous patients, using the serums of patients with granulomatous uveitis as controls. In the serology laboratory of the Johns Hopkins Hospital, a titer of 100 to 125 Todd units is regarded as a high normal, and a titer of 250 Todd units as definitely indicative of a prior streptococcal infection. Using these two titers as standards, our experiences with this test are summarized in Table 6.

Three of the highest titers recorded in the nongranulomatous uveitis group (titers of 500, 500 and 333 Todd units) were in patients who had received intravenous injections of streptococcal vaccines, a procedure which in itself will undoubtedly stimulate an increased antibody production. Our results are therefore in accord with the numerous other investigators who have explored this reaction in uveitis. While there is a slightly increased incidence of positive reactions in patients with nongranulomatous uveitis, it is so small that it is without statistical significance, and is certainly in marked contrast with the high incidence of streptococcal hypersensitivity found in the same patients. All that can be concluded is that the determination of the antistreptolysin-O titer is without value in the study of nongranulomatous uveitis. It is recommended that it be dropped from the Academy Survey.

E. The Rose-Heller test

This is a test for the so-called "rheumatoid factor," an abnormal gamma globulin constituent which agglutinates sensitized sheep erythrocytes. It is present in high titers in the serum of patients with rheumatoid arthritis, in some patients with collagen disease, but is usually absent in patients with ankylosing spondylitis, hypertrophic arthritis, and other forms of arthritis.

We have run this test in 22 patients with nongranulomatous uveitis and in 11 patients with granulomatous uveitis. In the nongranulomatous group it was positive in seven cases, an incidence of 33 percent. However, five of these patients had rheumatoid arthritis, and whether the other two were in the presymptomatic stage, or had incipient collagen disease was undetermined. The test was negative in all 11 of the patients with granulomatous uveitis, none of whom had any arthritis.

From this very limited experience, it

TABLE 6

Antistreptolysin-O titers in patients with nongranulomatous and granulomatous uveitis

Type of Uveitis	No. of Cases	No. and % with Titers 100(+)T.U.	No. and % with Titers 250(+)T.U.
Granulomatous	26	6 or 25%	0 or 0%
Nongranulomatous	27	10 or 37%	5 or 18%

would appear that this test is also without value in the diagnosis of nongranulomatous uveitis, and there is no indication for its further investigation in this disease.

F. Buffy coat smears

This is a test for the presence of lupus cells in the blood. When positive, it is regarded as directly indicative of the specific collagen disease. The test requires examination of the smears by a trained hematologist, and is relatively expensive. Several negative examinations are necessary before the possibility of lupus erythematosus cells can be ruled out.

We have employed this examination in 19 patients, all with nongranulomatous uveitis, in whom other examinations had aroused the suspicion of possible collagen disease. In one case it was positive—a patient with probable early lupus erythematosus. On repeated examinations, one typical lupus cell was found. In the other 18 patients the smears were negative. Since this test is so consistently negative in nongranulomatous uveitis, there appears to be no reason to explore it further in the routine uveitis survey.

G. Cephalin flocculation and thymol turbidity

These are primarily tests for an impaired liver function. However, since they are believed to be dependent on an abnormal gamma globulin fraction in the blood serum, it appeared they might be worthy of investigation. Accordingly, from 1956 to 1958, these tests were run on 32 patients, all with nongranulomatous uveitis. One patient showed a weakly positive cephalin flocculation and one other showed a thymol turbidity titer of 4.8 (high normal titer 4.0). The test was negative in 31 of the 32 patients examined. Since these tests appeared to have no relation to nongranulomatous uveitis, they were abandoned.

H. C-reactive protein

The C-reactive protein (CRP) test is for the detection of precipitins which flocculate in the presence of the nitrogenous carbohydrate-C polysaccharide of pneumococci. These precipitins appear in the blood serum after a variety of stimuli—bacterial infections, vaccine therapy, or indeed after any nonspecific fever-inducing insult.

The C-reactive protein of the blood serum in its relation to uveitis has been extensively investigated in the Research Department of the Wills Eye Hospital.[14,15] In the earlier studies a somewhat higher incidence of positive tests was found in the uveitis group than in the control group, but there was usually some associated systemic condition which could explain the positive tests. These investigators likewise found a higher incidence of positive tests, both in the blood serum and the aqueous, in patients with nongranulomatous uveitis than in those with granulomatous uveitis. As a result of their over-all experiences, it was concluded that patients with nongranulomatous iridocyclitis showed a slightly higher, but statistically significant, incidence of positive C-reactive protein reactions in the blood serum and in the aqueous than did patients with granulomatous uveitis or the normal controls. It was suggested that the C-reactive protein found its way into the aqueous through transfer across a pathologically altered blood-aqueous barrier rather than through actual intraocular formation. It was conceded that the reaction was without value as a diagnostic procedure in the differentiation of nongranulomatous and granulomatous uveitis in any particular patient. It was hypothesized that the stimulus arising from an inflammatory focus in the uveal tract was of insufficient intensity in itself to evoke the formation of the C-reactive precipitins in the blood serum and that, when it was positive in uveitis cases, it was usually due to some associated fever-inducing or inflammatory factor.

While we have made no detailed or systematic study of the C-reactive protein reaction in our etiologic studies of uveitis, we have employed it in a number of cases. Our

experiences almost exactly parallel those reported by the Will Eye Hospital group. The test is positive in a small number of patients with either nongranulomatous or granulomatous uveitis but, when positive, there is usually some associated systemic factor which adequately explains the positive results. We have observed no striking difference in the incidence of positive tests in the two types of uveitis, but on this point the number of cases is insufficient to be of any statistical value.

In view of the reports of the Wills Eye Hospital group, and our own more limited experience, the C-reactive protein reaction does not appear to be of any value whatsoever.

TABLE 7

NUMBER OF CASES AND PERCENTAGE INCIDENCE OF ETIOLOGIC FACTORS IN 432 CASES OF GRANULOMATOUS UVEITIS (1950–60)

Ascribed Etiology	No. of Cases	Percentage Incidence
Toxoplasmosis	133	30.9
Tuberculosis	94	21.7
Differential diagnosis (toxo. or tbc.)	29	6.7
Syphilis	20	4.6
Sarcoidosis	19	4.4
Brucellosis	21	4.9
Histoplasmosis*	17	3.9
Miscellaneous (viral, symp. ophth., etc.)	32	7.4
Undetermined (negative surveys)	67	15.5

* Tests for histoplasmosis in 186 patients only.

COMMENT

Our over-all experiences with the Uveitis Survey as outlined in the Academy *Brochure,* and performed with similar or with the actual antigens now furnished in the diagnostic kit, and with various other tests employed in the exploration of the general problem, may be summarized as follows:

1. No diagnostic test or laboratory procedure has as yet been found which in itself aids in the differential diagnosis between granulomatous and nongranulomatous uveitis.

2. In 432 cases of granulomatous uveitis (including 104 partial surveys) the recommended Academy procedures have yielded excellent evidence of the etiologic factor in 365 instances, and have been unsuccessful in 67 cases—an incidence of 84.5 and 15.5 percent, respectively. The actual etiologic diagnoses thus made are shown in Table 7.

Undeniably, some of these diagnoses were presumptive and based on tenuous evidence and others were actually erroneous. However, the subsequent course of these patients under therapy indicated the number of such mistaken diagnoses was small. In the cases in which the diagnosis lay between toxoplasmosis and tuberculosis, a therapeutic trial test with antitubercular agents usually established the correct diagnosis.

3. In 291 cases of nongranulomatous uveitis, a definite bacterial hypersensitivity was demonstrated in 233 instances—an incidence of 80 percent. In 218 cases this hypersensitivity was to the stock streptococcal vaccines in the diagnostic kit, and in 15 cases was only to autogenous organisms isolated from the patient's own systemic foci of infection. When due allowances were made for a hypersensitivity unrelated to the uveitis, the incidence of a demonstrated hypersensitivity apparently related to the uveitis was 64 percent.

These findings fully vindicate the value of the *Uveitis Survey.* They also show, however, that in an appreciable group of cases—15 to 22 percent in the group of granulomatous and 36 percent in the group of nongranulomatous uveitis cases—the survey as now constituted is inadequate to disclose the etiologic factor. It is also apparent that the present survey, which was originally designed solely for investigative purposes, is laborious, time-consuming, and expensive to the patient. This introduces two questions.

The first question is: How can the diagnostic kit be technically improved? The immediate answers to this are:

A. The present diagnostic kit can be improved by substituting new and more virulent strains of the alpha streptococci for the inert strains now furnished.

B. The five additional strains of the subgroup A of the beta streptococci should be added to the 42 strains now provided.

The second question deals with the practicability of the survey in the hands of the busy, practicing ophthalmologist, not primarily engaged in research. It may be phrased as follows: How can the labor be lightened, the time necessary for the survey be decreased, and the expense to the patient lessened—all with the purpose of bringing the survey more within range of the practicing ophthalmologist? Possible answers are:

A. In patients with a clear-cut definite granulomatous type of uveitis, the examinations for foci of infection and the tests for bacterial hypersensitivity may be omitted.

B. Since it is recognized that an acute, anterior, nongranulomatous uveitis may be the presenting symptom, and be secondarily superimposed on what is basically a granulomatous inflammation, it is wiser in all cases of nongranulomatous uveitis to retain the radiographic examination of the lungs and mediastinum, and the tuberculin, the toxoplasmin and the histoplasmin skin tests. In clear-cut, definite cases of nongranulomatous uveitis all other tests for systemic granulomatous disease can be omitted with only small danger of loss.

C. In patients with nongranulomatous uveitis, in whom the radiographic studies of the teeth and accessory nasal sinuses have been negative, and in whom the general physical examination has shown no evidence of dental, sinus, tonsillar, or urogenital disease, the dental, otolaryngologic, and urogenital consultations may be omitted.

D. There appears to be no way in which the tests for bacterial sensitivity either with the stock vaccines, or with autogenous organisms, can be abridged.

E. In cases in which a differential clinical diagnosis between granulomatous and nongranulomatous uveitis cannot be made, there is no option other than following out the full survey recommended in the Academy *Brochure*.

If these suggestions for shortening the *Survey* and making it easier for the practicing ophthalmologist are adopted, shortened report cards or forms could readily be provided for these minimum surveys for both granulomatous and nongranulomatous uveitis. From these report cards the value of such abbreviated surveys could be estimated.

For investigative purposes, it would appear wiser that research institutions continue to employ the full survey in all cases of uveitis and thus add to our data on the relative value of the examinations and tests. It is also manifestly their duty to continue the search for hitherto unrecognized causes of granulomatous uveitis, for new and as yet unsuspected allergens which may be the cause of the responsible hypersensitivity in nongranulomatous uveitis, to explore further the highly important question of the role of both pathogenic and symbiotic viruses and of endotoxins in the etiology of both types of uveitis, to investigate the pathogenesis of many as yet poorly understood ocular reactions, to develop and evaluate new and also the older diagnostic procedures. These are all part-and-parcel of the continuing investigations of the absorbing problem of the etiology of endogenous uveitis. One of the chief functions of the present diagnostic survey is to make available to ophthalmic clinics and to the practicing ophthalmologist the knowledge already gleaned and the tools and procedures for which the value has already been demonstrated.

Summary

The results observed with the Academy *Uveitis Survey* in 328 cases of granulomatous and 297 cases of nongranulomatous uveitis, are reported and analyzed. The relative value of the several examinations, sensitivity tests, and laboratory procedures recommended are discussed. Also discussed are various other laboratory procedures which have been ex-

plored from time to time in the investigation of the etiology of uveitis.

In the over-all picture, the Academy survey has permitted a probable etiologic diagnosis of 78 to 84 percent of the patients with granulomatous uveitis and 64 percent of those with nongranulomatous uveitis. It is believed these results fully vindicate the value of the survey.

Certain technical recommendations are made for the improvement of the present diagnostic kit. A few suggestions are made whereby in certain clear-cut cases of both granulomatous and nongranulomatous uveitis, the survey might be shortened and thus made more useful to the practicing ophthalmologist and nonresearch ophthalmic clinics. Should these suggestions be adopted, it is believed there would be but slight scientific loss, and the practical value of the survey might be considerably enhanced.

The Johns Hopkins Hospital (5).

References

1. Woods, A. C.: The modern concepts of the etiology of uveitis. Am. J. Ophth., **50**:1170, 1960.
———: Endogenous Uveitis. Baltimore, Williams & Wilkins, 1956.
———: Endogenous Inflammations of the Uveal Tract. Baltimore, Williams & Wilkins, 1961, in press.
2. Guyton, J. S., and Woods, A. C.: The etiology of uveitis: A clinical study of 562 cases. AMA Arch. Ophth., **26**:983, 1941.
3. Woods, A. C., and Guyton, J. S.: The role of sarcoidosis and of brucellosis in uveitis. AMA Arch. Ophth., **31**:469, 1944.
4. Woods, A. C.: The use of specific streptococcus vaccines in nongranulomatous uveitis. AMA Arch. Ophth., **50**:129, 1953.
5. Woods, A. C., Jacobs, L., Wood, R. M., and Cook, M. K.: A study of the role of toxoplasmosis in adult chorioretinitis. Am. J. Ophth., **37**:163, 1953.
6. Woods, A. C.: A further study of streptococcus vaccines in nongranulomatous uveitis. AMA Arch. Ophth., **56**:749, 1956.
7. Catterall, R. D.: The aetiology and treatment of uveitis. Tr. Ophth. Soc. U. Kingdom, **78**:523, 1958.
8. Jewett, H.: Personal communication.
9. Jacobs, L., Naquin, H., Hoover, R., and Woods, A. C.: A comparison of the toxoplasmin skin test, the Sabin-Feldman dye test, and the complement-fixation reaction for toxoplasmosis in various forms of uveitis. Bull. Johns Hopkins Hosp., **99**:1, 1956.
10. Woods, A. C., and Wahlen, H. E.: The probable role of benign histoplasmosis in the etiology of granulomatous uveitis. Am. J. Ophth., **49**:205, 1960.
11. Jacobs, L., and Lunde, M. N.: An hemagglutination test for toxoplasmosis. J. Parsitol., **43**: 308, 1957.
12. Lunde, M. N., and Jacobs, L.: Characteristics of the Toxoplasma hemagglutination test antigen. J. Immunol., **82**:146, 1959.
13. Harley, D.: Allergic aspects of iridocyclitis. Tr. Ophth. Soc. U. Kingdom, **72**:419, 1952.
14. Wolkowicz, M. I., Hallett, J. M., and Leopold, I. H.: C-reactive protein in ophthalmology. Am. J. Ophth., **41**:942, 1956.
15. Wolkowicz, M. I., Hallett, J. W., Leopold, I. H., Feria, Q. A., and Wijewski, E.: Nonspecific tests in uveitis. Am. J. Ophth., **48**:502, 1959.

THE INFLUENCE OF CYCLOGYL® AND NEOSYNEPHRINE® ON TONOGRAPHIC STUDIES OF MIOTIC CONTROL IN OPEN-ANGLE GLAUCOMA

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Despite recent important advances in the treatment of glaucoma, miotic therapy is still the favorite control method for simple open-angle glaucoma. The mechanisms of miotic control are controversial but of interest. Factors which affect the efficiency of miotic control are certainly of practical as well as academic importance.

The present work compares the tonographic effects of Cyclogyl,® a parasympatholytic drug, and Neosynephrine,® a sympathomimetic drug, on the intraocular pressure and facility of outflow in eyes under miotic therapy for open-angle glaucoma. According to Becker and associates,[1] in open-angle glaucoma controlled by miotic therapy, dilatation of the pupil with Neosynephrine® usually does not raise the intraocular pressure and usually does not lower the facility of outflow. This investigation was prompted by our interest in the effect of a parasympatholytic drug on the intraocular pressure and facility of outflow of open-angle glaucoma during miotic therapy.

SUBJECTS

All patients had open-angle glaucoma under treatment with miotic therapy only, without any carbonic anhydrase inhibitor therapy. Two of the patients were being treated with Phospholine Iodide,® six with pilocarpine, and one with Humorsol.®

METHOD

The tonograms were made with a Mueller electronic tonometer and recorder. Recordings were made at the same time of day and the right eye was always measured first. Determinations were obtained three to five days apart for each patient, and all patients remained on their preset miotic therapy throughout the period of investigation.

Neosynephrine® was added to the miotic regimen by instillation of three drops of a 10-percent solution one hour before tonography. The parasympatholytic drug, Cyclogyl,® was added as a one-percent solution to the miotic therapy in the same manner as the Neosynephrine.® In all of these instances the pupils measured five to six mm. in diameter at the time of tonography.

RESULTS

The intraocular pressure, facility of outflow and the P_0/C values were analyzed as to their changes under the three conditions of the investigation: that is, miotic therapy alone, miotic therapy with Neosynephrine® (a sympathomimetic and mydriatic drug), and miotic therapy with Cyclogyl® (a parasympatholytic and cycloplegic drug).

Addition of Neosynephrine® to miotic therapy produced no consistent trend in the alteration in the intraocular pressure. However, some elevations and some depressions of intraocular pressure were recorded. Another study of the effects of phenylephrine in open-angle glaucoma (but without miotic therapy) has demonstrated variations in pressure and "C" value after instillation of phenylephrine.[2] Addition of Cyclogyl® caused increases of from 3.0 to 22 mm. Hg in the intraocular pressure in 12 out of 17 eyes (table 1). Of the remainder, three eyes had only a slight rise in pressure, one had no change in pressure, and one eye had a decrease in pressure. However, the addition of Cyclogyl® to the miotic regimen caused

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TABLE 1

INTRAOCULAR PRESSURE IN MM.HG UNDER THE VARIOUS DRUG REGIMENS

Patient		Medication			Miotic Used
		Miotic Regimen	Miotic Regimen with 10% Neosynephrine® Added	Miotic Regimen with 1% Cyclogyl® added	
M. P.	R	25	18	15	0.25% Phospholine Iodide®
	L	22	25	22	
J. D.	R	14	15	22	0.25% Phospholine Iodide
	L	16	21	28	
L. A.	R	16	15	27	2% pilocarpine
	L	26	21	34	
B. L.	R	18	19	27	4% pilocarpine
R. P.	R	23	27	24	0.25% humorsol
	L	21	24	22	
E. R.	R	20	17	30	0.5% pilocarpine
	L	22	20	30	
A. J.	R	21	25	23	2% pilocarpine
	L	22	25	26	
M. B.	R	19	20	22	2% pilocarpine
	L	17	17	23	
E. J.	R	23	30	45	2% pilocarpine
	L	36	32	45	

a consistent lowering of the tonographic "C" value in every case tested (table 2). It can also be seen that the lowering of the tonographic "C" in almost half of the cases was as much as 50 percent of the "C" while the patient was receiving miotic therapy alone. The addition of Neosynephrine® was followed by considerable variations in the tonographic "C" values, but there was no consistent trend in either raising or lowering the "C" value that would be significant in this small a series.

Neosynephrine® added to the miotic therapy produced no consistent trend in the alteration of the P_o/C ratio (table 3). There was an increase in six cases, a decrease in nine cases and in one case it produced no measurable change. The addition of Cyclogyl,® however, resulted in an increase in the P_o/C ratio in all but one eye in comparison with the values obtained with miotic therapy alone, and in every case in the investigation as compared with the values obtained with Neosynephrine® and miotics.

DISCUSSION

The fact that mydriasis with Neosynephrine® usually does not elevate the intraocular pressure and does not consistently reduce the facility of outflow in open-angle glaucoma (1) allows for its familiar use as an aid in the differentiation of narrow-angle vs. open-angle glaucoma, (2) permits its safe use as a mydriatic for fundus examination in open-angle glaucoma, and (3) points up the fact that the controlling effect of miotics in open-angle glaucoma is not related to pupillary size. On the other hand, use of Cyclogyl® (and probably cycloplegics in general) should require more caution in patients with open-angle glaucoma, as the facility of outflow is decreased with Cyclogyl® even if the condition is controlled on miotic therapy at the time.

The increase in the P_o/C ratio upon the addition of Cyclogyl® to miotic therapy further substantiates the interference of Cyclogyl® with miotic control of open-angle glaucoma. At this time it is not clear if this

TABLE 2

COEFFICIENT OF OUTFLOW UNDER THE VARIOUS DRUG REGIMENS

Patient		Medication			Miotic Used
		Miotic Regimen	Miotic Regimen with 10% Neosynephrine® Added	Miotic Regimen with 1% Cyclogyl® Added	
M. P.	R	0.25	0.28	0.15	0.25% Phospholine Iodide®
	L	0.19	0.21	0.13	
J. D.	R	0.25	0.38	0.13	0.25% Phospholine Iodide
	L	0.32	0.20	0.06	
L. A.	R	0.21	0.50	0.12	2% pilocarpine
	L	0.15	0.45	0.12	
B. L.	R	0.14	0.17	0.06	4% pilocarpine
R. P.	R	0.20	0.22	0.07	0.25% humorsol
	L	0.30	0.28	0.16	
E. R.	R	0.18	0.33	0.15	0.5% pilocarpine
	L	0.22	0.34	0.13	
A. J.	R	0.18	0.24	0.16	2% pilocarpine
	L	0.22	0.17	0.03	
M. B.	R	0.20	0.20	0.13	2% pilocarpine
	L	0.27		0.14	
E. J.	R	0.13	0.20	0.04	2% pilocarpine
	L	0.12	0.08	0.02	

effect from Cyclogyl® is mainly due to a "counteraction" of the miotic effect at one or more specific sites, or if there is an additional inhibitory effect on the drainage mechanism of the eye. Other variables, such as the secretion rate of aqueous and changes in scleral rigidity, must be considered.

Since Cyclogyl® probably counteracts all the actions of the usual parasympathomimetics used, one cannot say from this work alone which site of action of the miotics is most effective in increasing the facility of outflow. A number of investigations have been done which seem to point to the importance of ciliary muscle pull on the scleral spur in the miotic control of open-angle glaucoma. Fortin,[3] in 1929, demonstrated openly stretched trabecular meshwork in rapidly fixed eyes which had been treated with eserine. More recently, Flocks and Zweng[4] reported that the trabecular openings in monkey eyes are enlarged by pilocarpine, and McEwen[5] concluded that the diameter of the pores of the meshwork is probably the important factor in open-angle glaucoma. Furthermore, Armaly and Burian[6] found that the tonographic "C" value is greater when the eye is accommodating. Therefore, in our opinion, the finger of suspicion seems to point toward the action of miotic drugs on the ciliary musculature pulling on the scleral spur as the major location of its hypotensive action in the control of open-angle glaucoma.

There is certainly need for further investigation of the effect of these and other parasympatholytic and cycloplegic drugs on the "C" value in normal eyes, in early open-angle glaucoma, and in a larger series of open-angle glaucoma cases under miotic control.

SUMMARY

Tonographic studies were made on 17 eyes in nine patients with open-angle glaucoma controlled on various forms of miotic therapy. Tonographic studies were performed during miotic therapy alone, during miotic therapy with Neosynephrine® added, and during miotic therapy with Cyclogyl®

TABLE 3

P_0/C RATIOS UNDER THE VARIOUS DRUG REGIMENS

Patient		Medication			Miotic Used
		Miotic Regimen	Miotic Regimen with 10% Neosynephrine® Added	Miotic Regimen with 1% Cyclogyl® Added	
M. P.	R	100	64	100	0.25% Phospholine Iodide®
	L	112	112	117	
J. D.	R	56	40	117	0.25% Phospholine Iodide
	L	50	100	470	
L. A.	R	76	30	224	2% pilocarpine
	L	173	47	284	
B. L.	R	129	112	450	4% pilocarpine
R. P.	R	115	122	342	0.25% humorsol
	L	70	86	137	
E. R.	R	111	50	200	0.5% pilocarpine
	L	100	59	230	
A. J.	R	117	104	144	2% pilocarpine
	L	100	147	870	
M. B.	R	95	100	170	2% pilocarpine
	L	63		164	
E. J.	R	177	150	1,125	2% pilocarpine
	L	300	400	2,250	

added. Addition of Neosynephrine® to the miotic therapy had no consistent effect on the intraocular pressure or tonographic facility of outflow. Addition of Cyclogyl® to the miotic therapy usually resulted in an increase in the intraocular pressure over that with miotic therapy alone, and a decrease in the tonographic facility of outflow in every case tested.

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REFERENCES

1. Becker, B., et al.: The effect of phenylephrine hydrochloride on the miotic-treated eye. Am. J. Ophth., **48**:313-321 (Sept.) 1959.

2. Lee, P. F.: The influence of epinephrine and phenylephrine on intra-ocular pressure, A.M.A. Arch. Ophth., **60**:863-867 (Nov.) 1958.

3. Fortin, E. P.: Contributions a al solucion de las problumes del glaucoma. Arch. Oftal. Buenos Aires, **5**:219-230, 1931.

4. Flocks, M., and Zweng, H. C.: Studies on the mode of action of pilocarpine on aqueous outflow. Am. J. Ophth., **44**:380-386 (Nov.) 1957.

5. McEwen, W. K.: Application of Poiseuille's law to aqueous outflow, A.M.A. Arch. Ophth., **60**: 290-294 (Aug.) 1958.

6. Armaly, M. F., and Burian, H. M.: Changes in the tonogram during accommodation. A.M.A. Arch. Ophth., **60**:60-69 (July) 1958.

CHEMOTHERAPY AND AUTOLOGOUS MARROW TRANSPLANTATION IN PALLIATION OF MALIGNANT OCULAR TUMORS*

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This is a discussion of the new chemotherapeutic agents for symptomatic treatment of metastatic tumors of the orbit, with illustration of usage in three consecutive cases. If curative therapy of malignancy is planned, surgery or irradiation are the present methods of choice, but frequently are insufficient. Some forms of chemotherapy have been used for a number of years, for example, stilbestrol in prostatic carcinoma and sex hormones in metastatic carcinoma of the breast. The mechanism of action of these drugs is based on alteration of the environment of the tumor. ACTH or adrenal corticosteroids may also be of value in this respect, and may protect the bone marrow from drug toxicity.[1]

Recently there has been an exploration of medical therapy of cancer with a group of drugs which all simulate radiation to some extent. For instance, radioactive isotopes actually deliver ionizing radiation directly to the cell. A great number of other cytotoxic agents simulate radiation effect so much they have been termed radiomimetic. These may vary in their mode of action.

Alkylating agents (fig. 1) act by introducing a toxic bis, B-chloroethyl group into the nucleus of the normal and malignant cells.[2] Since malignant cells contain enzymes which release the B-chloroethyl group in larger amounts than normal, there is a selective nuclear inhibition of neoplastic cells, as well as some toxicity to all cells.[3] The prosthetic group (R) (fig. 1) functions by converting the B-chloroethyl group to an inactive transport form which is activated at the site of therapy. Among the available alkylating agents are nitrogen mustard, triethylene

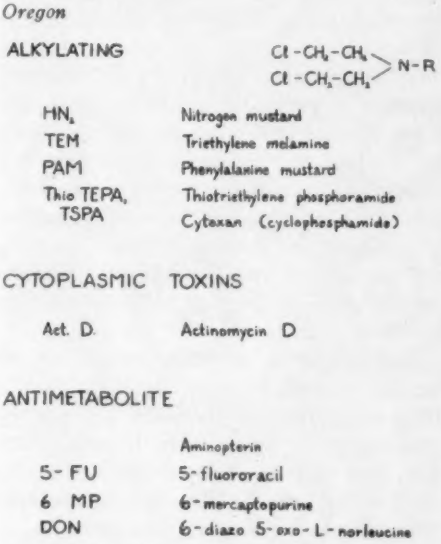

Fig. 1 (Burns). Cytotoxic agents.

melamine, phenylalanine mustard, thiotriethylene phosphoramide and cytoxan. These vary in their duration of action, with TEM and HN_2 having the shortest half-life, probably of only a few minutes,[4] and PAM and TSPA being active in the body for several hours.[5]

Other drugs, such as actinomycin D, originally isolated by Waksman[6] as an antibiotic from a strain of Streptomyces, may act directly on the cytoplasm of the malignant cell. This drug proved too toxic as an antibiotic. It can reactivate latent radiation effects, such as erythema and pigmentation, in tissues that have returned to normal appearance following irradiation.[7]

Certain antimetabolites may block specific enzymes producing metabolic arrest at sites essential to the growth of the cell. The antifolic acid drugs, such as aminopterin, prevent reduction of folic acid to folinic acid.[8] Folinic acid is necessary for formate transfer, a step in the synthesis of purines and

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pyrimidines, which are involved in nucleic acid production. The fluorinated pyrimidines, for example, 5-fluorouracil, presumably prevent the conversion of deoxyuridine monophosphate to the thymidylic acid of deoxyribonucleic acid. The antipurines, such as 6-mercapto-purine, interfere with the incorporation of purine, a component of nucleosides and nucleotides, into nucleic acid. Since the antifolic and antipurine drugs have different pathways of interfering with nucleic acid synthesis, they can be used synergistically. Glutamine antagonists, such as DON, act to prevent the donation of an amino group by glutamine to various biochemical reactions in the body.

Administration of these drugs can be classed as total body or regional. In total body usage, they may be given orally, intravenously or intramuscularly. If used regionally, they may be perfused through an isolated area of the body by passing the drug through a tumor-bearing area from the afferent artery to the efferent vein and recirculating the blood through a heart-lung machine. The regional technique seems ideal for localized tumors, since it can prevent harm to normal organs from the cytotoxic agent, which allows a much higher tumor dose of chemotherapeutic drug, and does not disturb the important host-tumor relationship. In addition, the oxygen content of the blood circulating through the heart-lung machine can be increased, which may increase the effectiveness of therapy.[9] The perfect regional technique in perfusion of artery and vein would be difficult in the ophthalmologic area, due to anastomoses between major vessels. Reese's[10] method of injection of TEM into the carotid artery seems an excellent compromise for ophthalmology, since the major effect of the drug is expended in a short time in the area supplied by the carotid artery.

All these drugs are toxic, not only to tumor but to other areas with a high rate of nucleic acid turnover: the bone marrow, causing anemia, leukopenia and thrombopenia; the gastrointestinal tract, with resultant nausea and vomiting, which can be controlled with antiemetic compounds, the gonads and basal layer of the epithelium.[2]

Bone-marrow toxicity can be ameliorated by use of the recently developed technique of autologous marrow transplantation. This consists of withdrawal of the patient's marrow before chemotherapy is started, with storage of the marrow outside the body in a plastic bag at refrigerator temperature during exposure to the toxic drug. The marrow remains viable and can be returned to the patient intravenously to repopulate the blood-forming elements which have been depleted by the antitumor drug.[11] Identical twin (isologous) or another human's (homologous) marrow has been used.[12] With prevention of marrow depression, it might be possible to give a larger dose of antitumor drug, or repeat doses at close intervals, for maximally effective therapy. Recently such massive chemotherapy has shown some promise.[13]

The technique of bone-marrow withdrawal is painful and would require general anesthesia in a child. It has been combined with intracarotid arterial injection of TEM* in two cases.

Case reports

Case 1

A white boy was in good health until two years of age when the parents noted a white reflex in the right eye (fig. 2). There was no family history of retinoblastoma. The eye was not enucleated until five months later, when pathologic examination revealed retinoblastoma with invasion of the

Fig. 2 (Burns). Case one—Creamy-white masses visible through pupil of right eye.

* Intravenous TEM supplied by C. H. Demos, M.D., Lederle Laboratories, Inc., Pearl River, New York.

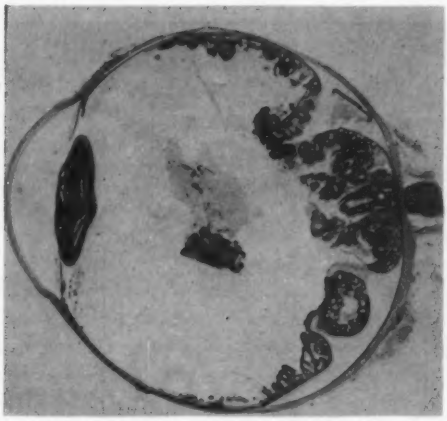

Fig. 3 (Burns). Case one—Horizontal section of enucleated right eye, showing retinoblastoma in two protruding masses medial and lateral to optic nerve, corresponding to elevations in Figure 2. Optic nerve contains tumor.

transected stump of optic nerve (fig. 3). Prophylactically, he was treated with 3,900 r of X-rays to the orbit.

He was well for 14 months, when swelling and discharge, thought to be due to infection, developed in the orbit. The implant became uncovered two months later and was removed one and one-half years after enucleation, at which time a biopsy showed recurrent retinoblastoma (fig. 4).

On hospitalization July, 1959, physical examination revealed a healthy, active four-year-old boy, weighing 27.75 lbs., who had a firm, nontender mass filling the right orbit (fig. 5). The lids did not blink and the child rubbed his right forehead as if in pain. X-ray films of skull, chest and long bones were normal. Cerebrospinal fluid contained no cells but a protein of 85 mg. percent. The blood count was normal, and in a bone-marrow biopsy there were cells suspicious of retinoblastoma. Despite the warnings of slight elevation of spinal fluid protein and suspicious cells in the marrow, it was elected to treat the patient with intracarotid TEM, modified by marrow transplantation and supplementary X-ray therapy.

Under general anesthesia 135 ml. of marrow was removed from the iliac crest, with heparinized syringes and needles, and refrigerated in a plastic bag. During this time the right carotid artery was exposed and 1.2 mg. intravenous TEM (based on a maximal dosage of 0.1 mg. per kg. of body weight[19] was injected into the artery. A cervical lymph node removed during this procedure was normal. Convalescence was uneventful, and the child's bone marrow was transfused intravenously the next day. Postoperatively, 2,400 r of radiotherapy was given to the orbit.

The blood count did not decrease below 4,550 WBC and 55-percent band neutrophils during the

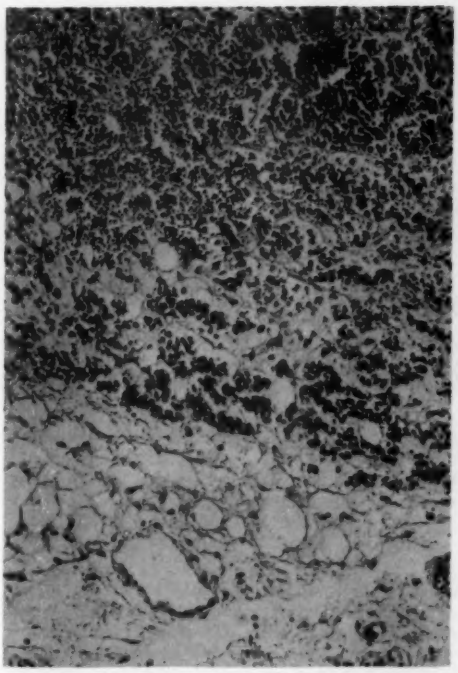

Fig. 4 (Burns). Case one—Wave of recurrent retinoblastoma cells invading orbital fat.

postoperative period (fig. 6). The platelet count one week after TEM was 26,000 but no other count was below 113,000. The swelling of the right orbit did not change until about 19 days after TEM and eight days after radiation was completed, when the

Fig. 5 (Burns). Case one—Anophthalmic right orbit with recurrent tumor bulging lids forward. Note protrusion compared to normal left eye. Markings of radiotherapy frontal port outlined on skin.

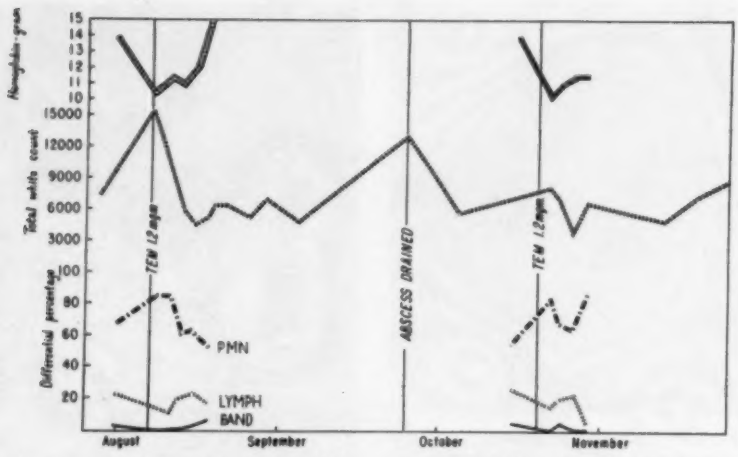

Fig. 6 (Burns). Case one—Blood counts during course of TEM chemotherapy. Note that each injection causes drop in hemoglobin (top), acute rise with subsequent drop of total white count (middle) and polymorphonuclears. Lymphocytes and band forms of polymorphonuclears drop immediately after injection, then rise.

mass began to shrink, the child ceased to rub his head, and the lids again could blink. The hair in the right occipital area fell out a week later in the area corresponding to the exit of X-rays.

The patient was readmitted for a repeat injection of TEM six weeks after the first. He appeared in good health, had gained 0.75 lb., and there was dramatic subsidence of the recurrent orbital mass. There was faint tanning of the skin of the eyelids. The orbital contents were atrophic without palpable masses. The bone marrow showed mild hypocellularity of the erythropoietic system and a dearth of megakaryocytes, but clot retraction was complete in one hour and the clot was of good quality. However, a stitch abscess was found in the previous incision and opening of the carotid artery was postponed. A lymph node removed when the abscess was drained was normal.

Three weeks later, the orbital mass had begun to recur as a firm nodular lesion, which never reached its original size (fig. 7). The patient appeared to be in slightly less good general condition, had headache, and again had begun to rub the orbit. He showed a tremor of the extremities, particularly notable on standing, and had lost weight. Under general anesthesia withdrawal of 130 cc. of marrow and intracarotid injection of 1.3 mg. TEM were performed. The marrow was infused intravenously the next day. Radiotherapy was begun two days postoperatively and an additional 2,050 r given.

A lumbar puncture was done after completion of X-ray therapy because of the tremor. Clumps of malignant cells were found in the cerebrospinal fluid, and the child was sent home, since he was comfortable. He remained in good condition for two months. The mass in the orbit again regressed completely. He ate well, maintained his weight, and blood counts were within normal limits. Suddenly, he became restless, began to vomit, coma and convulsions ensued and he died in four days.

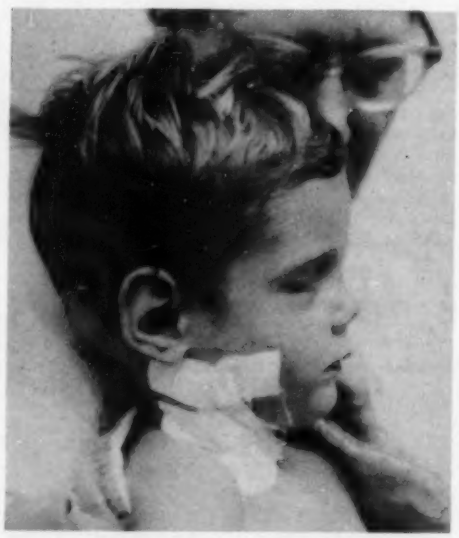

Fig. 7 (Burns). Case one—Early recurrence of retinoblastoma of orbit nine weeks after first, and immediately after second intracarotid injection of TEM. Note dressing on neck from cervical incision, slight portrusion of right eyelids (compare Figure 5) and localized right cervico-occipital alopecia at site of exit of X-ray.

Autopsy* revealed the right orbit to be free of tumor. The cause of death was hydrocephalus due to obstruction of the foramina of Luschka and Magendie by tumor tissue in the subarachnoid space extending from the pituitary fossa and optic chiasm around the midbrain and posteriorly into the medulla. There was necrosis of parts of the right temporal lobe of the brain, presumably secondary to the radiotherapy. Tiny foci of metastasis were found in the liver. The bone marrow was not examined but sections of lymph node and spleen were normal.

Comment. On the basis of this case, the role of TEM therapy cannot be evaluated. X-ray therapy alone could have caused the regression of the recurrent retinoblastoma of the orbit on two successive occasions, and TEM did not arrest the meningeal metastases. However, TEM in two maximal doses did not cause serious bone-marrow depression, although the effect of the treatment could be seen by the decrease in lymphocytes and band forms, with some leukopenia and thrombopenia, after both injections. After the first injection, there was mild depression of the red cell and platelet systems in the marrow. It is impossible to evaluate the protective effect of autotransfusion of marrow.

The treatment probably made his course less uncomfortable. The recurrent tumor caused no symptoms except tremor until the rapid four-day termination. This is in contrast to the probability of the lesion fungating out through the orbital opening, and the pain and size of the orbital recurrence decreased after each TEM-radiotherapy combined treatment.

CASE 2

A white girl was noted to have a white pupil at four weeks of age. One brother had retinoblastoma. She developed periorbital and conjunctival redness and a hazy cornea and was admitted to the University of Oregon Medical School Hospital, where enucleation was done for glaucoma of the right eye secondary to retinoblastoma. The tumor invaded the choroid, but not the optic nerve. At that time, a seven-mm. elevated yellowish-white tumor temporal to the left optic nervehead was found and treated with 4,600 r of X-rays through three ports.

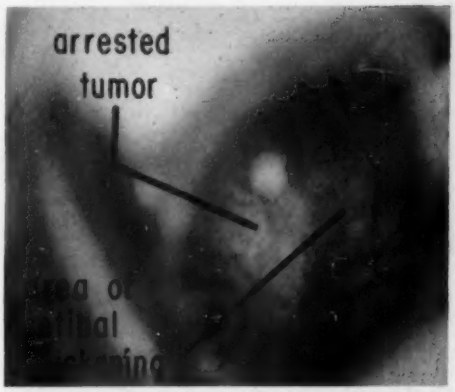

Fig. 8 (Burns). Case two—Photograph of elevated calcified mass of treated retinoblastoma, taken through contact lens under general anesthesia. Note grayish thickened area of retina between calcified mass (left) and blood vessel (right).

There was satisfactory regression of the tumor, which shrank to a white calcific mass.

Seven months after radiotherapy, examination showed a blurring of the superior border of the treated lesion with a greyish elevation of retina adjacent to the tumor. She was examined under general anesthesia one month later and a diagnosis of retinal edema was made (fig. 8).

On the next three examinations, at about monthly intervals, a progressive increase in size of the area of retinal elevation was described. The child was then lost to follow-up for two years, when she rapidly developed anorexia, weight loss, headache, vomiting and unsteadiness of gait. On readmission there were papilledema and stiffness of the neck, with X-ray evidence of increased intracranial pressure. The patient had a convulsion two days after admission.

Under general anesthesia, the next day, 120 cc. of bone marrow were withdrawn from the iliac crest and 1.3 mg. of TEM given into the left common carotid artery after a bilateral carotid angiogram. The marrow was replaced intravenously the following day. Following the angiogram and chemotherapy repeated convulsions and high fever developed. No relief was obtained with burr holes and ventricular tap, and the patient died two days later. No X-ray therapy was given.

Autopsy revealed extensive meningeal seeding of the tumor over the base of the brain which had caused internal hydrocephalus. The meninges of both optic nerves proximal to the chiasm were involved. There was regrowth of retinoblastoma adjacent to the calcified tumor in the left eye (figs. 9 and 10). The bone marrow, lymph nodes and spleen were normal. No pulmonary change was noted from marrow transplantation.

Comment. The intra arterial injection of

* Performed by John D. MacCarthy, M.D., Spokane, Washington.

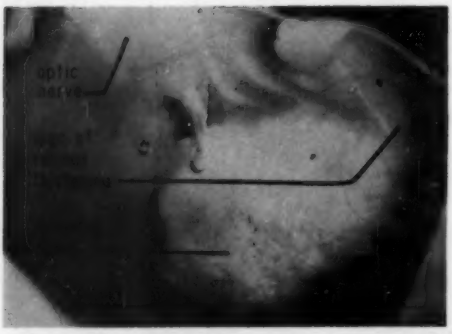

Fig. 9 (Burns). Case two—Gross photograph of opened left eye. Edematous optic nerve top left. On the right of the calcified mass is thickened area of retinal recurrence. Compare blood vessel far right with same vessel in Figure 8.

TEM, possibly combined with the bilateral cerebral angiogram, did not improve the child's condition and possibly hastened her death. The convulsive state, present before therapy, may have been increased by TEM, since alkylating agents may induce convulsions.[2] Injection of radioactive gold (Au^{198}) into the subarachnoid space may be preferable for subarachnoid metastases. However, she was lost to follow-up for such a long period of time that her condition was terminal on entry.

No destructive effect on the tumor cells in the left eye could be noted microscopically two days following the intracarotid injection of TEM, nor did the bone marrow show abnormality.

CASE 3

A five-year-old white boy developed constipation followed by pain in his left hip and abdomen. A 15 by 12 cm. left abdominal mass was found to be an inoperable neuroblastoma extending from the diaphragm to the pelvis, surrounding the aorta. He was treated with 3,000 r supervoltage X-ray therapy, without response. Three months later anemia and pulmonary and bony metastasis were present, and he was treated with blood transfusion and localized X-ray therapy. Five months after abdominal exploration the right eye became progressively more prominent and a clinical diagnosis of metastatic neuroblastoma of the orbit was made. The proptosis progressed until the cornea became exposed, the conjunctiva chemotic, and an exposure corneal ulcer, from which coagulase positive Staphylococci were cultured, developed (fig. 11).

When the child was hospitalized, it was not possible to suture the lids over the cornea. A total of 2,400 r of radiotherapy was given to a lateral orbital port, combined with nitrogen mustard 0.4 mg. per kilo intravenously, for a total of 7.0 mg. Three days later a hyopyon was present and the corneal ulcer was larger. On treatment with a

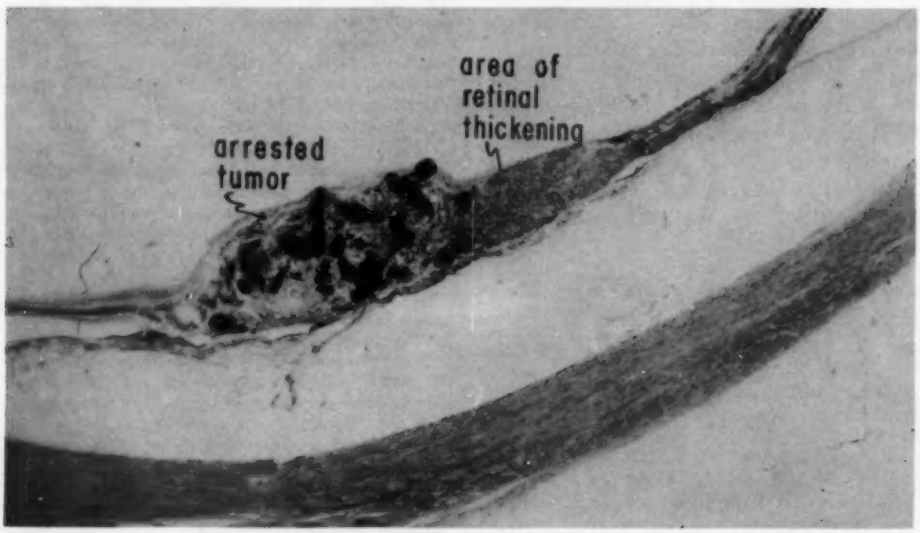

Fig. 10 (Burns). Case two—Posterior section of eye showing arrested retinoblastoma with large areas of calcium in necrotic tumor (left) and thickening of retina by recurrent viable tumor (right).

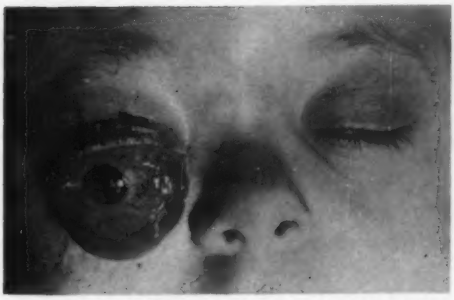

Fig. 11 (Burns). Case three—Proptosis of right eye on admission to hospital with exposure corneal ulcer.

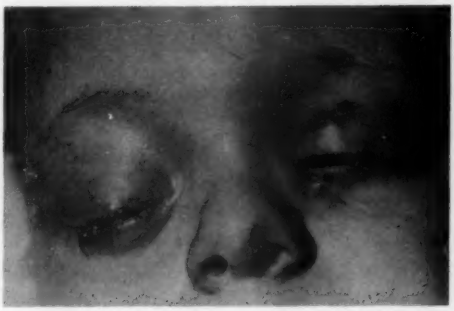

Fig. 12 (Burns). Case three—Almost complete regression of right orbital mass. Note ecchymosis left upper lid.

condensation shield, local and systemic antibiotics, the hypopyon cleared in 10 days, the corneal ulcer began to subside and the chemosis decreased. The exophthalmos remained about the same. An ecchymosis developed in the left upper lid and slight left exophthalmos was present. It was felt that minimal response to X-rays and nitrogen mustard therapy had occurred, but the upper lid covered the cornea two and a half weeks after beginning of treatment. At this point, 1,000 μg. of actinomycin D were given intravenously in divided dosage over the next five days.

One month after the start of combined therapy the eye was markedly improved, with only a small amount of chemosis below, the cornea was healed, but the globe was immobile. The left eye was unchanged. A week later the exophthalmos and chemosis had disappeared (figs. 12, 13 and 14) and ocular motility returned. The child said his eye no longer hurt. The cervical and cranial metastases, pulmonary and bony, continued to grow. Local radiation to the cervical nodes did not decrease their size.

After two and a half months of terminal hospitalization, the child died. At autopsy, metastases were widespread. The right orbit contained a calcified nodule of neuroblastoma, with necrotic cells, strikingly similar to the calcified retinoblastoma in Case 2. The early metastases of the left orbit were interesting in that there were perivascular infiltrates of tumor cells somewhat suggesting inflammatory infiltration. Presumably these perivascular lesions cause a breakdown of vessel wall resulting in the typical ecchymosis so characteristic of metastatic neuroblastoma."

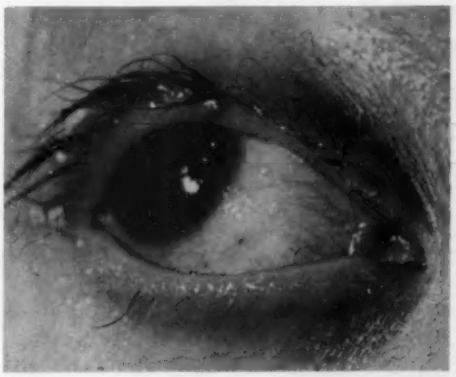

Fig. 13 (Burns). Case three—abduction of right eye.

Fig. 14 (Burns). Case three—Adduction of right eye. Note irregular light reflex of right cornea from scarring and ecchymosis of left upper lid.

Comment. It is difficult to assess the value of the different forms of palliative therapy in this case. X-ray therapy alone had minimal effect on the abdominal mass or the cervical metastases, but when given with nitrogen mustard and actinomycin D there was satisfactory regression of the orbital metastasis. Nitrogen mustard alone did not depress the tumor generally, nor did actinomycin D. Nitrogen mustard was chosen instead of TEM because of its longer action, and given intravenously instead of into the carotid artery because metastasis was wide-

spread throughout the body. Anemia was present from widespread bony metastases before chemotherapy was started, so autologous marrow transplantation was not done.

Discussion

It is apparent that the chemotherapy of malignancies is in its infancy. No one drug or mode of administration is best, and generally irradiation should be combined with the chemotherapy. Therapy requires the cooperative effort of a number of specialists: pediatrician, hematologist, surgeon, neurosurgeon, ophthalmologist.

It may be of ophthalmologic interest to explore chemotherapy of the commonest intraocular tumor, malignant melanoma. Recently striking results with regional perfusion of isolated malignant melanomas have been noted.[5]

In the described cases, there was palliation of orbital metastasis in Case 1 on two occasions, and in Case 3. Treatment did not affect meningeal metastases in Cases 1 and 2, and alkylating agent chemotherapy may have had an adverse effect in the second case, since the febrile and convulsive effect of the drug may have accelerated fatal termination of the disease.

Summary

1. A brief description of chemotherapy of malignant tumors is given.

2. Autologous marrow transplantation as a method of averting side-effects of antitumor agents is noted.

3. Therapy by these agents in three children with recurrent malignant ocular tumors is described.

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References

1. Wolcott, M. W., and Shaver, M. A.: Nitrogen mustard and adrenocorticotropic hormone in the management of patients with incurable carcinoma. Southern M. J., **52**:1375-1379, 1959.

2. Goodman, L., and Gilman, A.: The Pharmacological Basis of Therapeutics. New York, Macmillan Company, ed. 2, 1955.

3. Comparative clinical and biological effects of alkylating agents. Series of papers from Conference, March 28-30, 1957. Ann. N.Y. Acad. Sci., **68**:657-1266, 1958.

4. McAllister, R. M., Grunmeier, P. W., Coriell, L. L., and Blakemore, W. S.: A quantitative technique for the measurement of in vitro toxicity of 5-fluoro-2′ deoxyuridine (FUDR), nitrogen mustard (HN_2) and other antitumor agents. Cancer, **12**:938-943, 1959.

5. Creech, O. J., Krementz, E. T., Ryan, R. F., Reemtsma, K., Elliott, J. L., and Winblad, J. N.: Perfusion treatment of patients with cancer. J.A.M.A., **171**:2069-2075, 1959.

6. Waksman, S. A.: The Actinomycetes, Vol. I: Nature, Occurrence and Activities. Baltimore, Williams & Wilkins, 1959.

7. D'Angio, G. J., Farber, S., and Maddock, C. L.: Potentiation of X-ray effects by actinomycin D. Radiology, **73**:175-177, 1959.

8. Burchenal, J. H.: Chemotherapy of cancer. Modern Medicine, April 1, 1960, pp. 145-154.

9. Austen, W. G., Monaco, A. P., Richardson, G. S., Baker, W. H., Shaw, R. S., and Raker, J. W.: Treatment of malignant pelvic tumors by extracorporeal perfusion with chemotherapeutic agents. New England J. Med., **261**:1037-1045, 1959.

10. Reese, A. B., Hyman, G. A., Tapley, N. duV., and Forrest, A. W.: The treatment of retinoblastoma by X-ray and triethylene melamine. AMA Arch. Ophth., **60**:897-906, 1958.

11. Wilson, R. E.: Technics of human bone marrow procurement by aspiration from living donors. New England J. Med., **261**:781-785, 1959.

12. Thomas, E. D., Lochte, H. L., Jr., Cannon, J. H., Sahler, O. D., and Ferrebee, J. W.: Supralethal whole body irradiation and isologous marrow transplantation in man. J. Clin. Invest., **38**:1709-1716 (Oct.) 1959.

13. Jack, G. D., Doyle, L., and Palejwalla, M. M.: Tretamine in the treatment of inoperable lung cancer. Lancet, **1**:206-207 (23 Jan.) 1960.

14. Reese, A. B.: Tumors of the Eye. New York, Hoeber, 1953.

PROGNOSIS OF SECONDARY GLAUCOMA FOLLOWING RETINAL ARTERY OCCLUSION*

WITH THE REPORT OF AN INTERESTING CASE

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Duke-Elder[1] states that, "complications of (retinal) arterial obstruction are few. . . . A secondary glaucoma has *rarely* occurred. . . ." Indeed many experienced ophthalmologists profess never to have seen secondary glaucoma following retinal artery occlusion.

In recent years, however, a number of reports[2-7] have appeared in the literature, and there seems to be little doubt that secondary glaucoma following retinal artery occlusion is a specific entity. Wolter, et al.[3,4] have reported upon three cases within the past two years, indicating that this condition is probably not as uncommon as has been thought. Within the past year at least four articles[5-7] on this subject have appeared in the literature. Perraut and Zimmerman[5] reported on six cases and gave an excellent review of the literature; they state, "treatment of this secondary glaucoma is generally unsuccessful, and the eye is frequently enucleated soon after the onset of ocular pain."

It is our dual purpose to focus attention specifically on the prognosis in this distinct form of secondary glaucoma and to add a rather unusual case to the growing number of such cases being brought to our attention.

* From the Wills Eye Hospital.

PROGNOSIS

Reported to date have been 33 patients who have had secondary glaucoma following retinal artery occlusion; one of these[8] had bilateral glaucoma following a diagnosis of bilateral retinal artery occlusion. In all, there have been 34 eyes affected (table 1). Of these, 27 (79 percent) were enucleated (20 within one month following the initial glaucoma symptoms). One patient[7] refused enucleation despite a painful, stony hard eye; visual acuity was not mentioned in the report, but had been only hand movements in the involved eye before the onset of secondary glaucoma.

One patient[9] came to autopsy two months after the onset of glaucoma symptoms (one year after the occlusion). A second patient[10] came to autopsy three years after the arterial occlusion (? length of time after onset of glaucoma); there was no light perception in the affected eye at the time of death.

Two of the remaining four eyes were in

TABLE 1

REPORTED CASES OF SECONDARY GLAUCOMA FOLLOWING RETINAL ARTERY OCCLUSION

	No. of Eyes	Visual Acuity	Symptoms
Enucleated	*27 (79%)	—	—
Nonenucleated	6 (21%)	—	—
a. autopsy	†2		
b. other	5		
		1. ?	Painful, "stony hard" eye (enucleation refused)
		2. No light perception	Controlled on miotics
		3. No light perception	Pain controlled with retrobulbar alcohol
		4. No light perception	Rendered pain free by iridectomy (tension 40–50)
		5. ?	Periodic "intolerable pain" ("tic? arteritis?")
Total	34		

* Twenty of the 27 eyes enucleated within one month following initial glaucoma symptoms.
† One autopsy within two months following glaucoma, other autopsy three years after occlusion (no light perception).

the same patient;[8] neither eye had light perception. One eye was maintained on miotic therapy, but pain in the other eye necessitated control with retrobulbar alcohol injection. Another patient's eye[2] had a tension that could not be brought below 62 mm. Hg (Schiøtz). There was no light perception. An ab externo iridectomy was performed and the eye was pain free, although the ocular tension was never lower than 40 to 50 mm. Hg (Schiøtz). The remaining patient was presented[11] to the Chicago Ophthalmological Society as a problem in management. The pupil of the affected eye was widely dilated in spite of miotic therapy; the tension was 27 mm. Hg (Schiøtz) (as compared to 15 mm. Hg in the unaffected eye). No mention was made of the visual acuity. Periodic episodes of "intolerable pain" were considered to be due either to "arteritis" or a "type of tic douloureaux."

It can be seen, then, that treatment is not generally but, rather, universally unsuccessful—at least concerning cases appearing in the literature; the majority of cases ended in surgical enucleation; with the possible exception of two, the remaining eyes had no light perception. The summary of the case presented before the Chicago Ophthalmological Society made no mention of the patient's visual acuity; episodes of "intolerable pain," apparently trigeminal in nature, make it seem likely that the pain was directly related to the secondary glaucoma present. The other patient whose visual acuity was not mentioned in the published case report had refused enucleation recommended because of intractable glaucoma.

Case report

A 49-year-old white man noticed suddenly poor vision. Upon reporting to Wills Eye Hospital (July 16, 1959) he stated he seemed to be looking at things as though through "frosted glass."

Physical findings were: Visual acuity, R.E., 6/6. Visual acuity, L.E., 6/6 (but visual acuity O.S. dropped precipitously if fixation wavered even slightly). Finger tension was normal in both eyes.

External ocular examination was within normal limits except for a sluggish pupillary reaction in the left eye to direct light. The consensual light reaction was brisk.

Ophthalmoscopic examination revealed the fundus of the right eye to be completely normal. No cilioretinal artery was present. Examination of the left eye revealed a normal disc, but there was marked narrowing of all branches of the central retinal artery with blanching of the entire fundus except for a normal appearing lower half of the macula and the fundus immediately below—this area being supplied by an intact, patent cilioretinal artery.

Slitlamp examination revealed deep anterior chambers with no evidence of anterior segment disease in either eye.

The patient was immediately given a retrobulbar injection consisting of one cc. of priscoline and one cc. of four-percent procaine. He was also given a dose of 500 mg. of Diamox intravenously and 100 mg. of Solu-cortef intravenously. CO_2 (five percent) inhalations were used for five minutes every 20 minutes.

The remainder of physical examination revealed a well-developed, well-nourished white man in no acute distress. Blood pressure was 130/80 mm. Hg. Aside from a grade-two systolic murmur in the aortic area, physical examination was within normal limits.

Past history was significant in that the patient was a rather heavy smoker and that he was once told he had a "patent foramen ovale." There were no cardiac symptoms.

Laboratory studies were normal.

X-ray and fluoroscopy showed right ventricular hypertrophy. There was no hilar dance.

Treatment consisted of anticoagulants (heparin) and vasodilators (CO_2 inhalation, amyl nitrate). Retrobulbar injection was repeated several hours after admission. The patient was also placed on Diamox (250 mg. qid), Equanil (200 mg. bid) and was advised not to smoke.

The visual field, O.S., (fig. 1) revealed macular sparing corresponding to the area of supply of the cilioretinal artery and also a rather large temporal island to a 10 mm. white/1,000 test object.

After five days in the hospital the patient was discharged with slight subjective improvement. There was no objective improvement. Although the visual acuity in the left eye was 6/6, a slight shift in fixation resulted in markedly decreased vision as the light impinged on infarcted retina instead of the area of supply of the patent cilioretinal artery. Intraocular pressure was 9.0 mm. Hg (Schiøtz) in both eyes.

Eight weeks after the arterial occlusion (September 10, 1959) the patient suddenly developed severe pain in the left eye and was readmitted to Wills Eye Hospital. Visual acuity, R. E., 6/6. Visual acuity, L. E., 6/60. Tension; R. E., 12 mm. Hg (Schiøtz); L. E., 40 mm. Hg (Schiøtz). The left pupil was irregularly dilated and a mild edema of the cornea was present. Early rubeosis of the left iris was noted. Response to medical therapy was poor and the following day a peripheral iridectomy was performed with cautery applied to the posterior lip of

the scleral incision (sclerotomy by cautery). There was a moderate amount of operative hemorrhage. A week after surgery the patient was discharged from the hospital; the anterior chamber was formed and there was a filtering bleb above. The lower third of the anterior chamber was filled with hemorrhage.

There were two subsequent episodes of pain with elevated tension in the left eye for which the patient was placed on miotics and then on a carbonic anhydrase inhibitor.

Six months after the arterial occlusion and four months after the onset of the secondary glaucoma the patient was on Carbachol (1.5 percent qid, but taken somewhat erratically) and Cardrase (125 mg. bid). Visual acuity: O.D., 6/6; O.S., 6/21-1 (pinhole 6/21 + 2.) Tension: O.D., 8.0 mm. Hg; O.S., 40 mm. Hg. The pupil of the left eye was dilated and fixed with an iridectomy at 12 o'clock. Slitlamp examination, O.S., revealed fine keratic precipitates. The iris was atrophic and rubeosis was present. There were posterior synechias at the 11,- 1,- 3,- and 6-o'clock positions. There was pigment on the lens face with faint clouding of the lens. A filtering bleb was not present. Fundus examination of the left eye revealed the disc to be somewhat pale and atrophic looking. Several small round hemorrhages were present on the disc and the disc margins were minimally blurred. The arteries were definitely attenuated but the retina was of normal color and transparency. A few round scattered hemorrhages were present. Gonioscopy revealed what appeared to be a fine membrane with fine vessels passing in front of the trabecular meshwork. Visual field (fig. 2) showed only slight changes from the field obtained on the initial hospital admission.

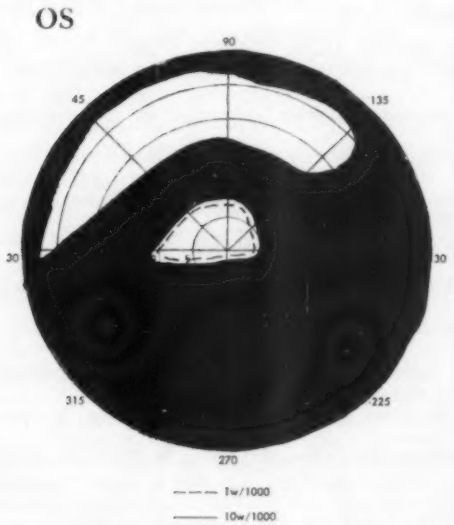

Fig. 1 (Weiss and Leopold). Visual field on July 17, 1959.

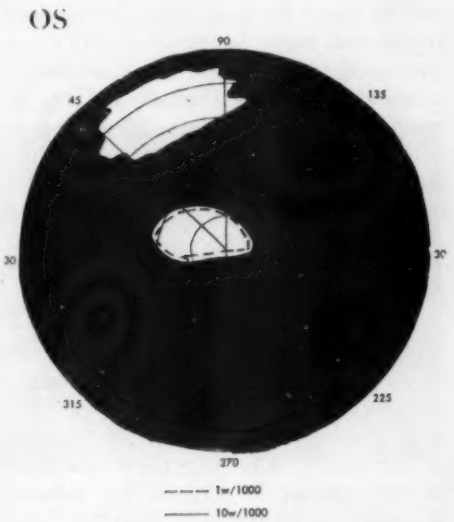

Fig. 2 (Weiss and Leopold). Visual field on February 11, 1960.

The other eye of this patient has an open angle and has never revealed any evidence of glaucoma by repeated visual field testing, tonometry, Schiøtz or applanation, tonography or water provocative testing. Cyclodiathermy is scheduled for the afflicted eye.

Discussion

We are all familiar with the fact that macular sparing due to a patent cilioretinal artery is occasionally seen in central retinal artery occlusion. Also, of late, an increasing number of cases of secondary glaucoma following retinal arterial occlusion have been appearing in the literature. However, there have been no cases reported in which an eye that had a spared macula then developed secondary glaucoma; this is such a case. The sudden onset of pain eight weeks after the retinal artery occlusion is typical of this type of secondary glaucoma, as is the refractoriness to medical therapy.

The therapy employed to restore central artery circulation failed. Retrobulbar priscoline and procaine, CO_2 inhalations, anticoagulant, fibrinolytic and anti-inflammatory agents all had no permanent effect. It certainly appears that some other approach

must be found for these cases. Perhaps local hypothermia might be considered and excessive amounts of oxygen simultaneously to reduce the tissue requirements and also increase the available oxygen. The effects of oxygen on the vessel caliber of the adult eye have not been significant and it might be helpful to the tissues deprived of a blood supply.

Certainly the therapy of the secondary glaucoma is unsatisfactory. This may be a glaucoma like that following central vein occlusion, if not identical. The best approach at present would be to attempt to restore circulation promptly and to avoid secondary venous closure and angle blockade. Perhaps we aid those closures that are transient and prevent permanent closure by reducing sludging and clot formation as well as lumen narrowing due to inflammation in the vessel walls. We may not be able to open clotted or embolus-closed vessel lumens or those due to organic vessel wall changes. Those central retinal artery closures secondary to permanent carotid artery insufficiencies may also prove resistant to all present therapy.

Once the glaucoma has developed, filtering procedures with minimal intraocular bleeding risk and cyclodiathermy offer the best chance for control.

Summary

Secondary glaucoma following central retinal artery occlusion is a distinct clinicopathologic entity.[3-6] There have been 34 eyes affected with this condition reported in the world literature. Approximately four fifths of these eyes were surgically enucleated; the remainder—with the improbable exception of two—had no light perception. The outcome of treatment has been universally unsuccessful in this condition.

A case was presented in which there was a central retinal artery occlusion with macular sparing due to a unilateral cilioretinal artery. A second catastrophe was then visited upon the "spared" eye in the form of a secondary glaucoma, the prognosis of which type of glaucoma has been universally and extremely bad. Treatment has been surgical and medical. To date, the affected eye still retains useful central vision.

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References

1. Duke-Elder, W. S.: Textbook of Ophthalmology. St. Louis, Mosby, 1941, v. 3, p. 2566.
2. Benton, C. D., Jr.: Glaucoma following occlusion of the central retinal artery. AMA Arch. Ophth., **49**:280-284, 1953.
3. Wolter, J. R., and Liddicoat, D. A.: Secondary glaucoma following occlusion of the central artery of the retina. Am. J. Ophth., **46**:182-186, 1958.
4. Wolter, J. R., and Phillips, R. L.: Secondary glaucoma following occlusion of the central retinal artery. Am. J. Ophth., **47**:335-340, 1959.
5. Perraut, L. E., and Zimmerman, L. E.: The occurrence of glaucoma following occlusion of the central retinal artery. AMA Arch. Ophth., **61**:845-865, 1959.
6. Holm, A., Sachs, J., and Wilson, A.: Glaucoma and retinal artery occlusion. Am. J. Ophth., **48**: 530-532, 1959.
7. Gupta, J. S.: Secondary glaucoma following occlusion of the central retinal artery. Brit. J. Ophth., **44**:52, 1960.
8. Ross, J. V. M.: Bilateral occlusion of the central retinal artery complicated by bilateral secondary glaucoma. EENT Monthly, **29**:561-563, 1950.
9. Manz, W.: Anatomische Untersuchung eines an Embolie der Arteria centralis retinae erblindeten Auges. In Festschrift für von Helmholtz. Hamburg & Leipzig, L. Voss, 1891, pp. 9-17.
10. Coats, G.: Obstruction of the central artery of the retina. Roy. Lond. Ophth. Hosp. Rep., **16**:262-306, 1905.
11. Holt, H.: Chicago Ophthalmological Society (Proceedings). Am. J. Ophth., **34**:1760-1761, 1951.

UVEITIS WITH SECONDARY RETINAL ARTERIOSCLEROSIS*

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In 1958, a type of arteriosclerosis occurring after retinal vein obstruction was described before this society.[1]

With capillary and venous stasis, arterioles, especially of the first, second and third order become dilated, develop a more brilliant, burnished reflex and are called copper wire. Arteriosclerotic plaques sometimes appear on such arteries in the absence of complete vein obstruction. These are yellowish-white, glistening thickenings of the outer arteriolar wall. They have sharply demarcated borders and a predilection for bifurcations, bends in the arterioles and a-v crossings. Such plaques completely or partially hide the blood column from view and at times appear to have a crystalline content. They do not interfere with vessel patency and may disappear in time without residual evidence of their presence. These lesions are not primarily intimal and as Cogan[2] stressed they should not be confused with atheroma.

With the onset of complete vein obstruction, similar but much more extensive lesions develop in regional arteriolar walls (fig. 1). Considerable lengths of the blood column may be completely hidden, visible as a thin thread, or patchily visible as a very irregular ribbon. Characteristically the arteriosclerotic wall is yellow-white, dense, sharply demarcated, coarsely granular and at times contains crystalline deposits. Neither arteriosclerotic plaques nor these longer sclerosed segments have been seen on normal arterioles. The vessel elsewhere is always burnished and copper wire, and veins are hidden at a-v crossings by the thickened arteriolar wall. At the ragged ends of this pipestem sclerosis, a clear zone between the normal edge of the blood column and the terminal tip of the sclerosis suggests an adventitial beginning of the process.

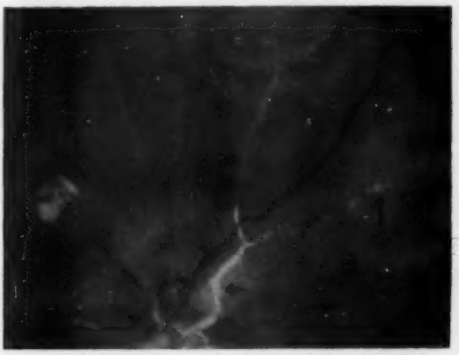

Fig. 1 (Wise). Classic secondary arteriosclerosis developing nine months after central retinal vein obstruction. Arrows indicate both uninterrupted and segmental distribution of arterial lesions.

Recently Griffin and Bodian[3] described three cases of posterior uveitis in young adult Negroes. Each showed segmental, periarterial, yellowish-white plaques. They appeared after the onset of the chorioretinitis, became most prominent at the height of the disease, and slowly faded as the inflammation subsided. All lesions fitted closely about the arteries. One "ensheathed the first division of the inferior retinal artery like a pair of pants." Usually arteries nearest the area of chorioretinitis were involved. However, their second case, with an inferior nasal inflammatory lesion, showed plaques on all arterial branches out to the second and third divisions.

It has been difficult to find adequate descriptions of this lesion in the literature. They have appeared casually inserted in articles on uveitis, tuberculous retinitis, metastatic retinitis, periphlebitis of Eales and even as an example of true periarteritis no-

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dosa. The lesion has been called periarteritis nodosa tuberculosa, retinal periarteritis, retinal arteriolitis, discontinuous reversible arteriopathy and, most recently, segmental retinal periarteritis.

Friedenwald,[4] in 1902, mentioned a rare form of white spots upon or to either side of retinal arterioles in three of 38 active cases of circumscribed exudative chorioretinitis. They were not further described.

Gowers,[5] in 1904, described a segmental thickening of the outer arterial coat as a rare manifestation of Bright's disease. He ascribed a similar "perivasculitis" in inflammatory conditions to an accumulation of leukocytes in the perivascular sheath.

Saganuma,[6] in 1927, and Shoji,[7] in 1930, noted periarterial white sheathing in cases suggestive of Eales' disease.

In 1929, Peters[8] described a case of metastatic uveitis with classic periarterial segmental plaques. The illustration was typical.

Kyrieleis,[9] in 1933 and again[10] in 1950, gave the first good description. His early report described one case of traumatic uveitis which developed multiple light-colored shields insetting retinal arterial walls. Some arteries were encircled like signet rings, giving a beaded appearance. They were common at bifurcations and one was extensive enough to convert a longer arterial segment into a narrow white stripe. These periarterial lesions slowly disappeared as the uveitis cleared.

He later reported six cases with similar scattered plaques on retinal arterioles during the course of uveitis. They appeared during the third week of inflammation and highly reflecting, glistening dots were seen in several of the older lesions. Indistinct sheathing of retinal veins was noted in one case.

Asayama,[11] in 1935, described such periarterial lesions in Harada's disease and Muncaster and Allen[12] reported what may have been this lesion in a case of bilateral uveitis.

Hesse[13] mentioned white arterial sheathing in a case of metastatic retinitis and Elwyn[14] cited Gresser's case of tuberculous chorioretinitis in which periarterial lesions resembled those described by Kyrieleis.

Dufour and Welter's case,[15] ascribed to periarteritis nodosa, was insufficiently typical as reported or pictured to be included.

Klien[16] described a typical case occurring in uveal disease. The illustrated, scattered, yellow, arteriolar plaques never changed position and slowly faded as the uveitis cleared. Van den Heuvel,[17] Friemann[18] and Thiel[19] also mentioned this periarterial lesion.

Case reports

The following cases will serve to illustrate points to be brought out in this report:

Case 1

A 30-year-old Puerto Rican man was admitted to Bellevue Hospital on November 7, 1959, with a five-day history of blurred vision, O.D. His past general and ocular history and his general physical examination were all negative.

O.D.: vision, 20/200. There were fine vitreous floaters, a small area of acute chorioretinitis at the macula and no other ocular change.

O.S.: vision 20/20. The eye was normal.

All etiologic studies were negative. He was given systemic steroid therapy but developed a dendritic corneal ulcer, O.D., and steroids were stopped. After this, the corneal ulcer spontaneously healed but the chorioretinitis became worse.

Six weeks after onset the right eye showed a few keratic precipitates and slight flare with cells in the anterior chamber but the pupil dilated well without synechias. Fine vitreous opacities were present but did not prevent a clear fundus view. The disc was hyperemic and the retina edematous, especially at the posterior pole. The central area of chorioretinitis was hazy with white strands extending into the vitreous. The veins were full, and slightly tortuous with a patchy, hazy, white, irregular cuffing. The arteries showed an increased reflex and a granular copper-wire change throughout but no true arteriosclerotic plaques were seen.

Three weeks later the anterior chamber was clear, the vitreous clearer and the macular lesion showed early pigmentation. In one very burnished area of the artery just above the macula was a glistening white dot, as has been described in older segmental plaques of this disease, but no actual plaques appeared.

Four weeks later there was further healing of the macular lesion, less retinal edema and the glistening dot on the superior temporal artery was gone. The disc was less hyperemic with early temporal pallor and the arteries were less burnished

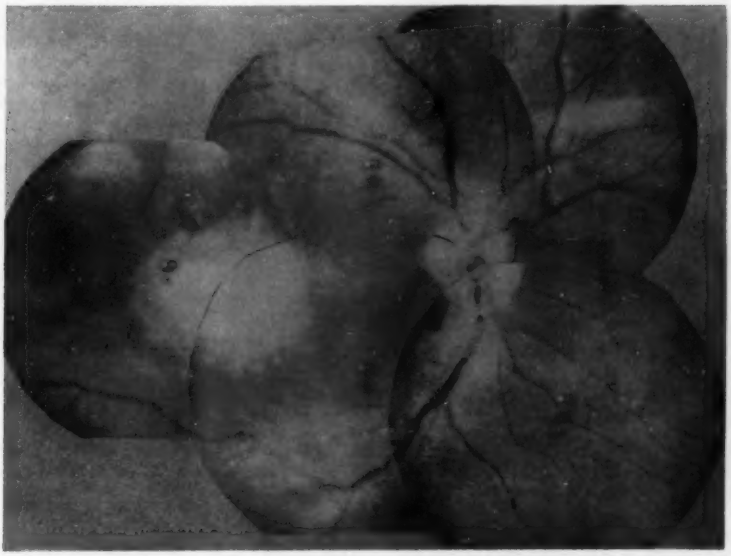

Fig. 2 (Wise). O.D. Case 2. See text for description.

but still showed copper-wire change and hid the venous blood column where they crossed it.

This case of acute central chorioretinitis therefore demonstrated associated retinal periphlebitis and its attendant circulatory stasis, retinal edema, copper-wire arterioles and even a brilliant dot on one artery in a very burnished area, but no true arteriosclerotic plaques.

CASE 2

A 29-year-old man had had convulsive disorder of unknown etiology for many years. His past eye and general history were otherwise negative. In early December, 1958, he suddenly developed blurred vision of the right eye.

Examination one month later showed the following:

O.D.: corrected vision, counts fingers at one foot. There were small keratic precipitates, a mild flare and a few cells in the anterior chamber. Stringy and clumped vitreous floaters were present, arising from an oval, hazy white lesion at the macula. Early pigment proliferation was seen at its border and adjacent retinal traction lines were visible. There were a few scattered hemorrhages about the macula. The disc was hyperemic, the veins dark and full, with the halo sheathing in the far periphery only and several well-developed a-y nicks posteriorly. The arteries showed an increased reflex and burnishing. On all arteries, especially the temporal branches there were scattered plaques and rings of hazy, yellowish adventitial change. An artery just above the macula had an irregular moth-eaten coat about its blood column (fig. 2).

The left eye had normal vision and was negative except for the fundus. The veins were full and the arteries showed a slightly increased reflex. A superior nasal vein in the periphery was halo sheathed, becoming markedly so and very narrowed at a bifurcation where it divided into normal-appearing branches. The lower branch looped toward and disappeared into a heavily pigmented scar in the nasal periphery (fig. 3). This scar had a central gray-white area with extension of tissue in a loop over the pigmented border to normal retina.

The patient was hospitalized and complete study was negative except for a positive toxoplasmosis skin test and a dye titer positive in a 1:256 dilution.* Skull X-ray films were negative for intracerebral calcification.

The chorioretinitis subsided slowly and several brilliant crystalline deposits developed in some arterial plaques.

Dr. Roberto Buitrago of Managua, Nicaragua, reported the inflammatory lesion quiet on May 1, 1959. Most periarterial white spots had disappeared but a few faded ones were still present.

CASE 3

A 38-year-old Panamanian with no previous eye history developed blurred vision, O.S., on April 1,

* All dye titer tests were performed in the laboratories of the National Institute of Health, Bethesda, Maryland.

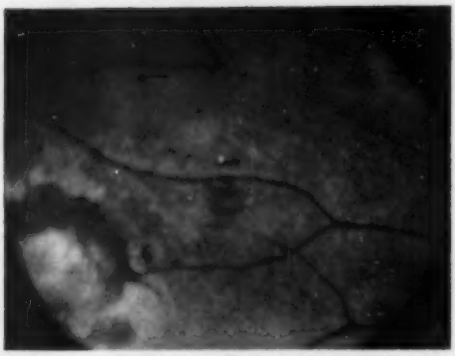

Fig. 3 (Wise). O.S. Case 2. See text for description. Arrows indicate probable direction of blood flow in the obstructed vein.

1959. He had had nonspecific urethritis in 1954 persisting two years before full recovery. On admission to Bellevue Hospital April 30, 1959, his eye examination was as follows:

O.D.: vision 20/20. The eye was completely normal.

O.S.: vision 20/200. The anterior chamber showed a mild flare and a few cells but the pupil dilated well without synechias. There were large and fine vitreous floaters. The disc was hypermic and widespread retinal edema was present. The veins were dilated and dark. Both uniform halo sheathing and scattered, irregularly broadened, fuzzy white periphlebitic foci were present. These two types of venous sheathing were most marked posteriorly but extended in a lessening degree to the periphery. There was an area of circumscribed subacute chorioretinitis just above the horizontal meridian midway between the disc and macula. Pigment proliferation appeared at its lower border and fuzzy, white strands extended from it into the vitreous. A venous branch passing through the lesion showed heavy periphlebitic sheathing. The macula was edematous with gray-white spots on the retinal surface and yellowish fatty exudates formed a macular wing between the fovea and the patch of chorioretinitis. This lay in the drainage area of the small macular vein so heavily involved with periphlebitis that its blood column in places was not visible. The arteries throughout showed an increased burnished reflex and a classic arteriosclerotic plaque ensheathed the superior temporal artery as it passed near the area of chorioretinitis. Significant laboratory studies were: a negative Mazzini, a 1.0 + positive tuberculin skin test in a dilution of 1:10,000,000, a 3.0 + positive toxoplasma skin test and a positive toxoplasma dye titer in a dilution of 1:1024.

He was treated with intravenous ACTH and later systemic steroids. By May 9, 1959, the inflammatory lesion was subsiding with increasing pigmentation. On either side of the superior temporal arteriosclerotic plaque were two patches of neovascularization and a few microaneurysms.

By July 7, 1959, the vision had returned to 20/20, the vitreous was clearer and the chorioretinitis definitely healing. The neovascularization and aneurysms near the sclerotic plaque had disappeared and the plaque was fading. Elsewhere arteries were still burnished and obscured the veins at crossings. A delicate white strand appeared extending from the temporal disc, preretinally, in a curve toward the lesion. Although no associated vessels were visible, it was interpreted as a delicate fibrotic proliferans from the disc toward the hypoxic area of inflammation.

On December 1, 1959, the anterior segment was normal, the vitreous clear and the chorioretinitis healed. The arteriosclerotic plaques had disappeared but the arteries were still burnished throughout and most brilliant in the area of the lesion. All veins appeared completely normal.

Case 4

A 38-year-old Italian man with completely negative past eye and general medical history noted hazy vision of the left eye three weeks prior to his first examination. On February 19, 1959, his vision in each eye was 20/20 and O.D. was completely normal.

The left eye had anterior chamber flare, cells and a few fine keratic precipitates. The pupil dilated well without synechia and the vitreous revealed many fine and a few larger floaters. There was retinal edema in all quadrants, more marked up and nasally. Here, several disc diameters from the disc was a small area of active chorioretinitis. Adjacent to it was the superior nasal artery which in this area was completely sheathed by a fuzzy yellowish-white pipestem coating, completely hiding the blood column. Just laterally, a superior vein was irregularly narrowed. Beyond this narrowing it was dark, dilated, beaded and had halo sheathing, indicating obstruction. Other veins throughout the fundus were dark and dilated only. There were fuzzy, yellow-white, scattered arteriosclerotic plaques on both arterial branches to either side of the chorioretinal area and also on a small artery passing temporally on the disc. A brilliant crystalline dot appeared in the most heavily sclerosed arterial segment. Between the obstructed vein and the area of chorioretinitis a patch of aneurysms and neovascularization was noted (fig. 4).

All etiologic studies were negative except for a toxoplasmosis dye titer positive in a 1:8,000 dilution.

Because of the size and position of the chorioretinitis no treatment was undertaken.

Five weeks later resolution began. Several arteriosclerotic plaques now demonstrated brilliant crystal-like reflections and a new patch of rete retinitis proliferans developed just peripheral to the chorioretinitis.

On May 8, 1959, with further healing, the retinal edema was less, most arteriosclerotic plaques had disappeared and the previously obstructed vein was of normal caliber and color without evidence of halo sheathing. The neovascularization and

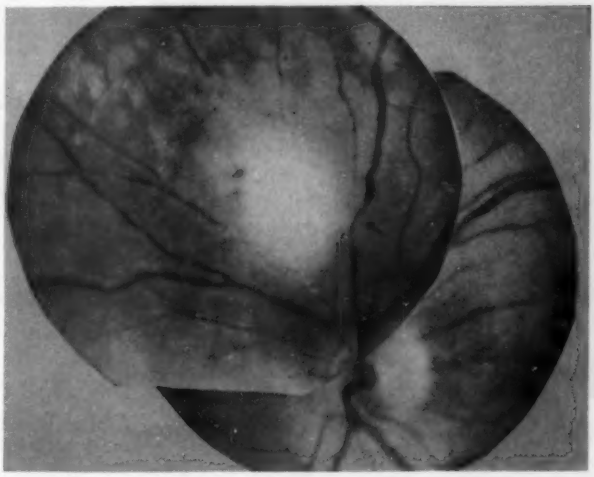

Fig. 4 (Wise). O.S. Case 4. See text for description. Arrow indicates site of vein obstruction.

aneurysms had disappeared. The extended sclerosis of the artery passing through the lesion was now patchy and here and there the blood column was again visible through it (fig. 5).

The retinal reaction gradually subsided in the year of observation. On February 25, 1960, there were still a few patches of arteriosclerosis on the most involved artery and all arteries had a mild burnished copper-wire appearance hiding the veins at crossings. A strand of avascular white tissue arose from the temporal disc and arched back to the retina toward the area of chorioretinitis which was now almost quiet (fig. 6).

On June 4, 1959, the Toxoplasma dye test was positive in a 1:8,000 dilution and on February 25, 1960, in a dilution of 1:1,024.

CASE 5

A 43-year-old Negro developed hazy vision September 7, 1959. He was admitted to a Philadelphia

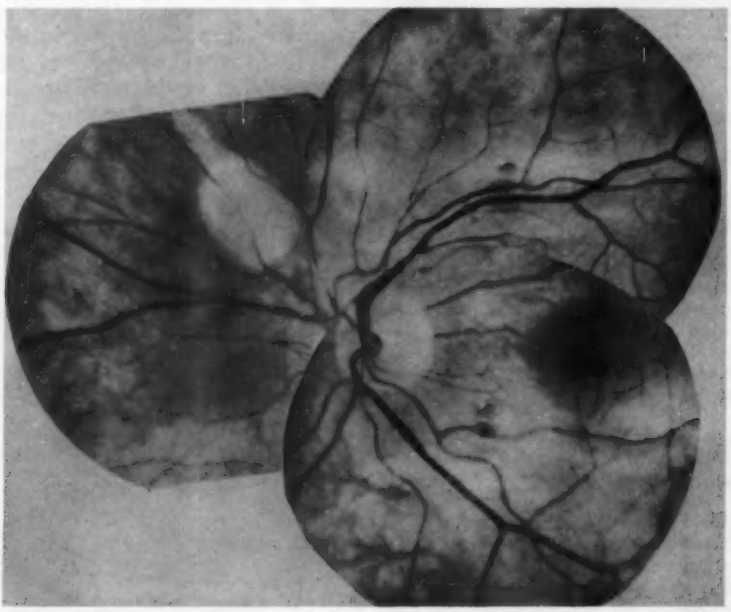

Fig. 5 (Wise). O.S. Case 4. Three months after Figure 4 was taken. See text for description.

Fig. 6 (Wise). O.S. Case 4. One year after Figure 4 was taken. See test for description.

hospital and treated for two weeks with ACTH, antibiotics, para-aminosalycilic acid and isoniazide with slight improvement. His diagnosis there was bilateral uveitis of undetermined etiology.

Shortly after his arrival in New York his eye condition worsened and he was admitted to Bellevue Hospital on October 8, 1959.

His past history revealed gonorrhea adequately treated on two occasions, four previous hospitalizations for bronchitis and pneumonia and a family history of tuberculosis. His tuberculin skin test was mildly positive and chest X-ray films revealed pleural thickening on the right. The diagnosis of active tuberculosis was not established. He had no cardiovascular disease and his blood pressure was 120/80 mm. Hg. Exhaustive etiologic studies were negative including those for syphilis, toxoplasmosis and sarcoidosis.

The vision, O.D., was hand movements at one foot; O.S., 20/30.

The right eye showed a severe uveitis with flare, cells, keratic precipitates and posterior synechias. There were heavy strands, fine opacities and a little blood in the vitreous. The disc was hyperemic; the retina edematous and elevated slightly in places. The veins were full, tortuous and dark. All four major arteries showed diffuse, white, arteriosclerotic pipestem sheathing, completely hiding the blood column from view, from the disc well out toward the equator.

The left eye showed a much milder uveitis and two active disc-sized patches of chorioretinitis down and temporally. The disc was hyperemic, the retina edematous, the veins full, tortuous and dark and the arteries slightly burnished, but no arteriosclerotic plaques were seen.

While on intensive steroid therapy, bilateral herpes corneae developed. The right eye was treated with iodine cautery, the left untreated, and both healed with the cessation of steroids. When steroids were stopped, the uveitis became worse and the interior of the right eye was not subsequently seen.

Case 6

A 44-year-old Negress* was transferred from the New York Eye and Ear Infirmary to Bellevue Hospital December 1, 1959. She had a most severe uveitis in both eyes. Intensive etiologic studies at both institutions failed to demonstrate the cause of her disease.

Examination revealed a vision of 15/200, O.D., and light perception only, O.S. Both globes were white but there were old keratic precipitates, mild flare and occasional cells in the anterior chambers, heavy posterior synechias and early lens opacities in each eye. The vitreous in the right eye was quite hazy and so cloudy in the left that the fundus could not be seen.

The right fundus showed fibrovascular proliferans from a hyperemic disc, dark, dilated veins with suggestive sludging in one, periphlebitic focal white spots along veins with a classic, acute inflammatory vein obstruction at one such site on the inferior temporal vein. Retinal hemorrhages were scattered in the area of venous drainage beyond this point. Secondary arteriosclerosis was suggested but was insufficiently well seen to be sure. In spite of all treatment her disease was progressive and shortly the right fundus could not be seen.

This patient showed such a degree of venous stasis and obstruction that retinitis proliferans was well developed.

Discussion

These arterial wall lesions had all the characteristics of the secondary arteriosclerosis previously described after vein obstruction. Their slightly fuzzier appearance with the ophthalmoscope was due to the inflammatory vitreous opacities and was considerably obviated by slitlamp examination.

Perivasculitis and perivascular sheathing are terms which have been indiscriminately used to describe different lesions about both arteries and veins.

Fuzzy, white, patchy cuffing of veins, extending well beyond the vein wall into adjacent retina and if severe, hiding the venous blood column from view has been histologically proven due to a collection of round cells about the vein[20–22] (fig. 7). The uniform white stripes of unvarying width beside the

* This patient was referred to me by Dr. Gerald B. Kara of New York.

hazy venous blood column have been shown microscopically by Ballantyne[23] to represent a lipohyaline change in the vein wall. This reversible lesion is characteristically present peripheral to a point of vein obstruction (fig. 8). Secondary arteriosclerosis after vein obstruction is the comparable arterial lesion to venous sheathing. It has, however, a very different clinical appearance. It has been shown due to hyalinization and fibrosis of the media and adventitia. Although no studies so far have been made, a lipid stain of such an arteriole wall should prove positive.

Knapp[24] stated unequivocally that the perivenous lymphocytic cuffing already described and seen in uveitis does not occur about arterioles except where arterioles pass through an area of perivenous pathology. A false concept of this appearance may be gained from ophthalmoscopic examination because hazy white clumps in the vitreous are mistakenly projected around arteries seen behind them. Slitlamp examination readily reveals their true position in the vitreous or on the retinal surface and not intraretinally about the artery. Retinal photographs enhance this misinterpretation of their actual position.

The periarterial lesions in uveitis have been described as stationary, transient, occurring on otherwise normal arterioles and always segmental in distribution. They have been considered due to an allergic reaction

Fig. 7 (Wise). Acute chorioretinitis with early perivenous round-cell accumulation.

Fig. 8 (Wise). Healed chorioretinitis with halo vein sheathing beyond the point of obstruction. Lipohyaline change in this vein wall.

of the arterial wall and explanation for their periodic distribution has been sought.

In no case of the present series did they appear on normal arterioles. The first case showed only diffuse, milder, arteriolar wall change. The arteries had a burnished, copper-wire appearance with thickened walls, increased reflex and hiding of the venous blood column at crossings. The very brilliant reflex at several bifurcations suggested that plaques might form momentarily but the chorioretinitis subsided too quickly. These arterioles became less burnished as the disease subsided but did not return entirely to normal, for at crossings the venous blood column remained hidden.

The next cases showed scattered plaques on diffusely copper-wire arterioles. The former seemed to fragment and disintegrate as they disappeared and always the artery was markedly burnished where the plaques had been.

The fifth case, being more severe, showed long uninterrupted stretches of secondary pipestem arteriosclerotic sheathing. The segmental distribution had become confluent.

The diffuse copper-wire arteriole represents the milder change. In severer cases a critical level is reached which triggers the opaque plaquelike deposits. This would be comparable to the sudden color change of a solution as a critical indicator level is

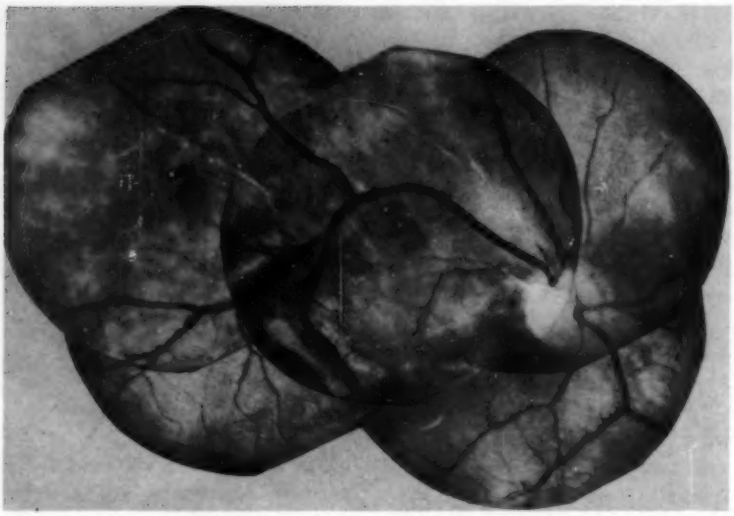

Fig. 9 (Wise). O.D., two years after obstruction of the superior temporal vein. See text for description.

reached. It is tempting to suggest deposition of lipid as the cause, for glistening, crystalline flecks are seen in these plaques. An indirect trigger mechanism, rather than a direct effect from the focal chorioretinitis, is also suggested by the presence of plaques on distant arterioles across the disc from the inflammatory lesion. Finally, the diffuse pipestem sclerosis seen in the more severe cases (Case 5) is also against a basic segmental concept.

How then can one accommodate an identical secondary arteriosclerosis after vein obstruction and also as a sequel of uveitis?

After branch vein obstruction, arterial blood still enters the capillary bed in the area previously drained by the now obstructed vein. Circulation does not, however, come to a standstill. It is simply slowed as individual red blood cells meander through the stagnant congested capillary bed until each reaches a channel directly drained by still patent venules. Thus the individual red blood cell circulation time on this circuitous course would be greatly lengthened.

Figure 9 shows the fundus of a 26-year-old woman with an obstruction of the superior temporal vein near the disc. This photograph was shown two years ago[1] as an example of secondary arteriosclerosis after vein obstruction. In this particular individual the sludged blood in the microcirculation of the obstructed region was readily visible with the retinal slitlamp. The slowed circulation time was obvious. As sludged red blood cells reached patent venules the speed of circulation increased, sludging disappeared and shortly the course was too rapid to visualize. Figure 10 shows this same fundus one and one-half years later. Note the development of fibrotic retinitis proliferans in this area of sludged circulation. Visual acuity was still normal and no vitreous bleeding had occurred.

If uveitis were to produce retinal capillary stasis or vein obstruction, then the develop- of secondary retinal arteriosclerosis in the course of this inflammation would be logical. There is both histologic and clinical evidence that uveitis does produce retinal capillary stasis and even vein obstruction. This in turn causes the delayed circulation time necessary for the development of secondary arteriosclerosis.

Fuchs[20] drew attention to the retinal peri-

venular accumulation of lymphocytes in uveitis. He believed toxins from the uveitis acting through the vitreous upon the retina cause venous dilatation and transmural migration of lymphocytes. With more severe processes the entire inner retinal layers were so affected.

Samuels[25] in a microscopic study of 59 cases of iritis serosa following surgery or trauma found round cells distributed along retinal capillaries and, especially, clustered lymphocytes about veins. These findings were particularly prominent at the posterior pole but were present well out toward the ora. The distribution along veins was irregular, forming heavy signet rings in some places.

Zeeman[26] found this same pathologic process about retinal veins in uveitis and noted in some cases marked round-cell accumulation about the central retinal vein, even extending behind the lamina cribrosa. He concluded that these changes indicated an interference with retinal circulation.

Klien[16] also found aggregates of lymphocytes and monocytes about retinal capillaries and venules in uveitis. She described extensive perivenular cuffing of round cells with narrowing of the venous lumen. There were also extensive cellular infiltrations along superficial retinal capillaries and those connecting the two major retinal capillary beds.

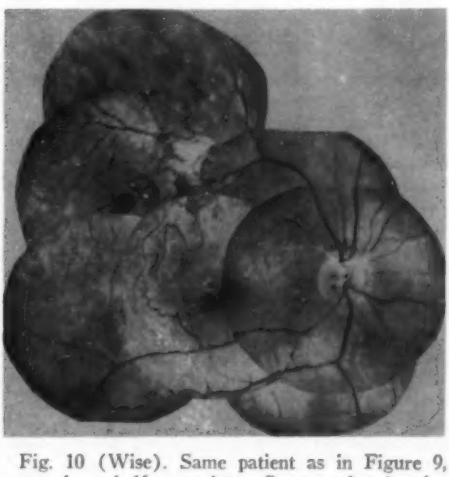

Fig. 10 (Wise). Same patient as in Figure 9, one and one-half years later. See text for description.

This pathologic picture indicates some toxic effects of the uveitis on thin-walled retinal capillaries and veins. It is almost inconceivable that such reaction could occur without coincident slowing of the circulation at the venous-capillary level. Both the presence of round cells microscopically and the clinical picture of these lesions denote a prolonged subacute process.

With careful slitlamp observation most of the retinal reaction in uveitis is similar to that seen after subsidence of the acute phase of central retinal vein obstruction. The widespread retinal edema is highly similar and the exaggeration of this with cystic change at the macula quite comparable. Even terminal macular pigment mottling occurs at times in both conditions. In both, the veins are dilated, more tortuous and dark, and halo sheathing of veins, though often transient in uveitis, is commonly present in both. Microaneurysms and both reté and fibrotic proliferans were visible clinically in cases here reported and Ashton[27] has shown microscopically that retinas in both conditions have innumerable microaneurysms. Finally, some uveitis cases show unequivocal branch vein obstruction, especially when the vein passes near or over the active chorioretinitic focus.

Pietruschka,[28] in an excellent report, summarized the sporadic literature on this subject. In his own carefully observed cases he pointed out the signs indicating obstruction to retinal venous outflow in uveitis. He concluded that the retinal changes seen in uveitis were more likely secondary to this venous outflow obstruction than to any direct retinal effect of the inflammation.

How do uveitis "toxins" reach the retina? Knapp,[24] Zeeman[26] and others believed that they passed directly at the ora to the retinal perivenular "lymph" spaces and thence back to the papilla. Strong clinical evidence that this does occur is gained from careful ob-

servation of the peripheral retina in cases of low-grade uveitis. The slitlamp and the Goldmann three-mirror contact lens are essential for these observations. Transvitreal "toxin" permeation also occurs for, in the absence of anterior uveitis, how else could a focus of chorioretinitis nasal to the disc cause temporal retinal changes? (Case 2); Peter's case;[8] Griffin and Bodian's second case.[3]

Thus it seems that uveitis "toxins" pass directly at the ora to the retinal perivenular spaces, or indirectly through the vitreous to the retina. These toxins effect an outpouring of round cells through the thin-walled retinal capillaries and veins. Coincident with this there is delayed retinal circulation time at this capillary-vein level. Some noxious product in such hypoxic retinal areas acts on regional arteries from without, producing external arteriosclerosis. This type of sclerosis has a strongly reversible tendency. It usually clears as the uveitis subsides and retinal circulation time is restored toward normal.

Summary

Certain cases of uveitis are associated with segmental yellowish-white plaques ensheathing retinal arterioles. These lesions are identical with a type of arteriosclerosis secondary to retinal vein obstruction described in 1958.[1] Their segmental character is deceptive for they occur only on abnormal arteries showing a milder degree of the same change throughout.

Through different mechanisms uveitis and retinal vein obstruction slow retinal circulation time. Some noxious influences in such hypoxic retinal areas act on the artery from without to produce arteriosclerosis. This type of secondary sclerosis is partially, if not completely, reversible.

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References

1. Wise, G. N.: Arteriosclerosis secondary to retinal vein obstruction. Tr. Am. Ophth. Soc., **56**:361-382, 1958.
2. Cogan, D. G.: Discussion of arteriosclerosis secondary to retinal vein obstruction. Tr. Am. Ophth. Soc., **56**:381-382, 1958.
3. Griffin, A. O., and Bodian, M.: Segmental retinal periarteritis. Am. J. Ophth., **47**:544-548, 1959.
4. Friedenwald, H.: Acute circumscribed exudative chorioretinitis. Tr. Am. Ophth. Soc., **9**:577-588, 1902.
5. Gowers, W. R.: Marcus Gunn's manual and atlas of Medical Ophthalmology. London, Churchill, 1904, ed. 4, pp. 14-15.
6. Suganuma, S.: Ueber die Entstehungsweise der Gefass-tuberkulose der Netzhaut. Arch. f. Ophth., **118**:443-453, 1927.
7. Shoji, Y.: Ueber die mit A. O. erfolgreich behaudelte Netzhaut entzundung mit weissen Flecken. Zugleich ein Beitrag zur Kasuistik der Retinitis tuberculosa. Klin. Monatsbl. f. Augenh., **85**:161-169, 1930.
8. Peters, H.: Metastase nach Schweinerstlauf im Auge. Klin. Monatsbl. f. Augenh., **48/83**:25-30, 1929.
9. Kyrieleis, W.: Ueber atypische Gefässtuberkulose der Netzhaut. (Periarteritis "Nodosa" tuberculosa). Arch. f. Augenh., **107**:182-190, 1933.
10. ———: Die diskontinuierliche reversible arteriopathie bei uveitis. Arch. f. Ophth., **150**:600-613, 1950.
11. Asayama, R.: Ueber eine seltsame Perivasculitis bei einer Art von idiopathischer Panuveitis Choroiditis diffusa acuta (Harada): Über Periarteritis nodosa. Zentralblatt, **34**:344, 1935.
12. Muncaster, S. B., and Allen, H. E.: Bilateral uveitis and retinal periarteritis as a focal reaction to the tuberculin test. Arch. Ophth., **21**:509-511, 1939.
13. Hesse, E.: Zur Klinik der Retinitis metastatica. Klin. Monatsbl. f. Augenh., **105**:601-613, 1930.
14. Elwyn, H.: Diseases of the Retina. New York, Blakiston, 1953, ed. 2, pp. 498-499.
15. Dufour, R., and Welter, S.: Périartérite retinienne et vasculite généralisée. Ophthalmologica, **129**: 316-321, 1955.
16. Klien, B. A.: Retinal lesions associated with uveal disease: Part I. Am. J. Ophth., **42**:831-847, 1956.
17. Van den Heuvel, J. E. A.: Precipitates on the vitreous. Ophthalmologica, **130**:191-200, 1955.
18. Friemann, Von W.: Beitrag zur Netzhautgefässreaktion bei Uveitis. Klin. Monatsbl. f. Augenh., **126**:129-133, 1955.

19. Thiel, R.: An attempted synopsis of the physiology and pathology of the systemic and ocular vascular systems. Lecture 6th Pan-American Cong. Ophth., Jan. 31-Feb. 7, 1960, Caracas. Caracas, Venezuela, Tipografia Italiana, C.A.

20. Fuchs, E.: Ueber veränderungen des Schnerven bei ektogener intraokularer Entzündung. Arch. f. Ophth., **91**:1-65, 1915.

21. Verhoeff, F. H.: Histologic observations in case of localized tuberculous chorioretinitis. Arch. Ophth., **1**:63-70, 1929.

22. Loewenstein, A., Michaelson, I. C., and Hill, J.: Retinal vasculitis of the young: a pathological report. Tr. Ophth. Soc. U. Kingdom, **66**:211-230, 1946.

23. Ballantyne, A. J.: The state of the retina in diabetes mellitus. Tr. Ophth. Soc. U. Kingdom, **66**: 503-543, 1946.

24. Knapp, A.: Retinal periphlebitis in the course of acute exudative choroiditis. Arch. Ophth., **26**:750-753, 1941.

25. Samuels, B.: Chronic postoperative or posttraumatic retinitis (retinitis serosa). Am. J. Ophth., **19**: 493-503, 1936.

26. Zeeman, W. P. C.: Ueber Netzhaut und Sehnervenleiden bei Iridocyclitis. Arch. f. Ophth., **112**: 152-186, 1923.

27. Ashton, N.: Retinal microaneurysms in the non-diabetic subject. Brit. J. Ophth., **35**:189-212, 1951.

28. Pietruschka, G.: Ueber Klinische Beobachtungen bei Iridozyklitis, insbesondere hinsichtlich der Fundus-veränderungen. Klin. Monatsbl. f. Augenh., **124**:309-326, 1954.

OCULAR CHANGES IN LINEAR SCLERODERMA*

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Linear scleroderma of the face, called in French, sclérodermie en coup de sabre, is a type of circumscribed scleroderma (morphea), which affects the skin of the face and scalp. Characteristically, this form of scleroderma is restricted to one half of the face (that is, the foci never extend beyond the median line) and has a slow but progressive course. Otherwise, it has all the features typical of scleroderma—initial induration and subsequent atrophy of the skin and underlying tissues. Consequently, the foci are depressed and, if the changes begin in childhood, they usually lead to disturbances of bone development and resulting facial hemiatrophy. If linear (sabre cut) scleroderma of the face develops in adulthood, it may leave various atrophic changes of the skin, subcutaneous tissue, muscles, and even, less frequently, osseous system, but usually leads to no such advanced atrophy as does idiopathic facial hemiatrophy.

As a variety of circumscribed scleroderma, linear scleroderma never involves inner organs. It therein differs essentially from diffuse scleroderma, although occasionally progressive and extensive changes may eventually affect almost the entire skin. Circumscribed scleroderma further differs from diffuse scleroderma in that vasomotor symptoms of the Raynaud type are absent. The course is more benign and changes may recede, often even spontaneously.

In this connection the view has been expressed that the two are essentially distinct diseases (Piper and Helwig, 1955). However, sensory chronaxy measurements, especially in the seemingly unaffected skin, reveal a distinct prolongation of the time of transmission of nervous impulses in both circumscribed and diffuse scleroderma (Jablonska, Bubnow, Lukasiak, 1957-a). This is characteristic and pathognomonic for scleroderma because it is observed in no other disease. In clinically doubtful cases, measurement of sensory chronaxy may be a very valuable diagnostic aid (Jablonska, Bubnow, Lukasiak 1957-b).

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Linear scleroderma of the face of the sabre-cut type, especially in the atrophic stage, may resemble very closely the Romberg type of idiopathic facial hemiatrophy. Cassirer (1912) favors an identical neurotrophic pathogenesis in both diseases. Wartenberg (1945) believes that sabre-cut scleroderma is an abortive form of facial hemiatrophy, which is a sequela of hereditary degenerative changes in the nervous system. A similar view is expressed by Stava (1959), since he believes that facial scleroderma leaves, in most cases, changes of the facial hemiatrophy type.

However, the views of these authors are challenged by Archamboult and Fromm (1932), who admit frequent similarity and even coincidence of the two diseases but see no evidence of their being identical.

Wolff and Ehrenclou (1927) believe facial hemiatrophy is no pathologic entity but a syndrome imbalance of higher autonomic nervous centers. It may, therefore, coexist with circumscribed scleroderma as well as with other pathologic conditions. Jablonska, Lukasiak and Bubnow (1958) support the view that facial hemiatrophy and sabre-cut scleroderma are two distinct entities, but emphasize close pathogenetic relationship between them. Changes of the facial hemiatrophy type may develop as a sequela of "sabre-cut" scleroderma of the face, which leaves when it has cleared—especially in children—distinct atrophy not only of the skin and subcutaneous tissue but also of muscles and bones (Schnyder 1956). Marchionini (1958) believes this type of scleroderma with secondary facial hemiatrophy should be distinguished from Romberg's idiopathic hemiatrophy.

In the atropic late stage of linear scleroderma of the face the clinical picture may be so much like Romberg's hemiatrophy that morphologic distinction becomes impossible. However, close observation of its course will reveal distinct differences. In hemiatrophy, the primary lesion is atrophy of deeper tissues which thereafter affects the skin, whereas in scleroderma induration and adhesion of the skin to the deeper tissues are primary, and atrophic changes, secondary. Useful aids in differential diagnosis may be histologic examinations, which reveal no sclerosis of the connective tissue in facial hemiatrophy, and measurement of sensory chronaxy which, unlike in scleroderma, is not prolonged in hemiatrophy (Jablonska, Lukasiak, Bubnow 1958).

Identification of sabre-cut scleroderma as an abortive form of facial hemiatrophy appears to be largely due to the fact that some of the cases described as hemiatrophy undoubtedly represent scleroderma (Wartenberg). However, whether the nosologic and pathogenetic distinctness of the two diseases is admitted or not, their pathogenesis is closely allied, and the mechanisms by which they are brought about probably depend on the higher autonomic nervous centers, with different degrees of involvement of the cerebrospinal (in hemiatrophy) or only spinal (in scleroderma, according to Korting and Korte, 1958) system.

Changes in the eyes may occur in either hemiatrophy or sabre-cut scleroderma depending on sympathetic system disturbances.

In sabre-cut scleroderma, the changes not infrequently involve the eyelids, which, like the surrounding skin, become indurated and atrophied and shows hyperpigmentation and depigmentations. The changes may extend to the deeper parts and lead to atrophy of tarsal plates, and may affect palpebral muscles, chiefly the levator, thereby causing ptosis. Occasionally there are pareses of other oculomotor muscles, for example, of the superior and medial recti (Cords, 1928). Lesions of the sympathetic nerve may lead to Horner's syndrome.

The cornea is seldom changed. Meunier and Toussaint (1958) observed diminished corneal sensitivity on the affected side.

Changes in the inner parts of the eye are little known so that there is no reference to them even in extensive dermatologic and ophthalmologic monographs. Available descriptions of particular cases are few and hard to find. Dolfus (1958) described in-

flammation of the anterior portion of the uvea which was complicated by clouding of the lenses and preceded by bilateral retinitis and optic nerve inflammation. However, this case was very complex, since the patient had congenital syphilis and died of intracranial hemorrhage two years after she had developed facial hemiatrophy.

Franceschetti, et al. (1958) described a unilateral Fuchs' syndrome without heterochromia. In this case, the skin changes were of the type seen in sabre-cut scleroderma but the authors say nothing definite on whether hemiatrophy or scleroderma should be diagnosed.

Changes in the eye fundus are referred to by Meunier and Toussaint (1958) and Dolfus (1958). Josten (1958) found in a patient he observed, retinal hemorrhages, newformed blood vessels in the optic disc, and tortuous venules. The general picture resembled thrombosis of the central retinal vein. However, in this case it is difficult to assess the causal link between ocular changes and co-existent scleroderma, since the former cleared after as little as two weeks, whereas sclerodermatous changes persist over many years.

Curtis and Jansen (1958) described an ipsilateral optic nerve neurocytoma with skin changes of the sabre-cut scleroderma type. In this case, that of a girl aged four years, the patient died and autopsy revealed hemorrhage into the lateral ventricle of the brain and changes of the type found in chronic arachnoiditis.

In idiopathic facial hemiatrophy, atrophic changes of eyelids and orbital tissues are the most typical. Dislocation of lacrimal points may cause lacrimation, lagophthalmos, and secondary changes in the cornea. The palpebral fissure may be narrowed. The eyeball is usually retracted and deeply set in the orbit (Osborne, 1922). There may be trigeminal neuralgias or, much less frequently, paralysis of the facial or oculomotor nerves.

Changes in the eyeball are exceptional. Lauber (1927) described changes left by subsiding uveitis, with a complicated cataract and eyeball atrophy on the side affected by hemiatrophy. Kahler (1881) described ill-defined changes in the eye fundus and deformation of the iris, which was pointed downward.

Classification of ocular symptoms in the diseases discussed in the literature is not quite reliable, since relevant findings do not always enable us to say whether the case described was one of linear scleroderma or of Romberg's idiopathic facial hemiatrophy (the cases of Kahler, Osborne, Franceschetti et al., and others). This hardly lends support to the theory that the diseases are identical but merely shows that no adequate distinction is made in diagnosis between linear scleroderma of the face with secondary atrophy and idiopathic hemiatrophy of the Romberg type.

The case to be described is entirely typical of the sabre-cut type of linear scleroderma. In the literature available to us we have found no description of the eye changes which occurred in this case.

Case report

The patient, Reverend M. P., aged 43 years, complained of skin induration on the forehead, which had appeared one year and a half earlier and gradually extended toward the scalp, eye-socket and cheek. The hair of the indurated area of the scalp initially became grey and then fell out. Some months before the changes appeared the patient was exposed to serious nervous strain and felt general weakness just before the present disease.

The first ocular complaints slightly preceded skin changes, which consisted of redness and edema in the region of the right eye. He called at the Ophthalmological Clinic of the Lodz School of Medicine, where meticulous examination failed to reveal any ocular changes other than conjunctivitis. A check-up on teeth and sinuses revealed no changes, and puncture of sinuses gave negative results. Since that time there has been only redness of the conjunctivas. Otherwise the patient has had no complaints regarding the eyes and sees well.

The patient remembered only children's diseases (measles and mumps) and influenzas and an undefined febrile disease at the age of 38 years which lasted about one month.

General examination revealed no perceptible abnormalities.

Skin changes concerned the face and scalp on the right side. They represented bandlike indurations near the median line in the scalp and somewhat to the right on the forehead and cheek (figs.

Fig. 1 (Segal, Jablonska and Mrzyglod). "En coup de sabre" scleroderma in the scalp. Hair is completely lacking within the focus. The skin is smooth, taut, and atrophied.

1 and 2). These indurations were completely hairless and somewhat depressed below the level of the surrounding skin. The cutis was here indurated, smooth, glossy and of alabaster tint; it could not be pinched. On the periphery of the indurations a lilac ring could be seen.

Small and not yet typical foci of the type of initial changes were present on the right cheek. The entire right side of the face appeared as if it were somewhat smaller, the forehead particularly so.

Investigations. Differential blood count and sedimentation rate, normal. Serologic tests, negative. Liver function tests, negative. In protein fractions merely fairly conspicuous hypergamma globulinemia (gamma—1.53 gm. percent in 3.33 gm. percent of total globulin; total protein 7.2 gm. percent, albumins 3.87 gm. percent).

Sensory chronaxy was prolonged in the entire normal skin of the body to 1.5 sigma, in indurated foci to 5.0 sigma, and on the peripheries of the foci to 2.5 sigma (normal values maximum 0.6 sigma). Capillaroscopy showed no abnormalities.

Radiograms of skull, normal. Maxillary sinuses somewhat opaque, the other sinuses unchanged.

Histologic examination of forehead skin. The picture is typical for scleroderma. The epidermis is considerably thinned and the dermal papillae flattened. There is hyperpigmentation of the basal layer and the underlying connective tissue is compact, homogeneous and sclerosed. Skin appendages are largely atrophied and the lumina of the vessels narrowed. No inflammatory infiltrations were revealed (fig. 3). Weigert staining showed normal elastic fibers within the entire corium and their absence in hyalinized foci. Only in the upper strata of the corium were there compact bundles of elastic substance resulting from collagen degeneration (fig. 4). These types of change in the elastic tissue are frequently found in scleroderma localized on the face or other areas exposed to sunlight.

Neurologic examination showed no changes in the nervous system.

Ophthalmologic examination. RIGHT EYE. Vision, 5/5. Tension, 18 mm. Hg. Eyelids and eyeball were normally set and mobile. There was insignificant superficial hyperemia of conjunctiva. The cornea was lustrous, corneal sensitivity preserved but slightly below that of the left eye. On Descemet's membrane there were a few grayish, dustlike, roundish deposits. The aqueous humor of the anterior chamber showed a Tyndall phenomenon. The iris had normal trabeculae but was, perhaps, slightly puffy. In the region of the 9:30-o'clock position, a sectoral atrophy of mesodermal layers of the iris with atrophy of trabeculae was visible. It was narrower in the parapupillary region and wider toward the periphery. In the affected region, the iris was depigmented and whitish and the blood vessels tortuous and distinctly visible as a reticule. The pupil was distorted, without synechias, and pointed in the direction of the 9:30-o'clock posi-

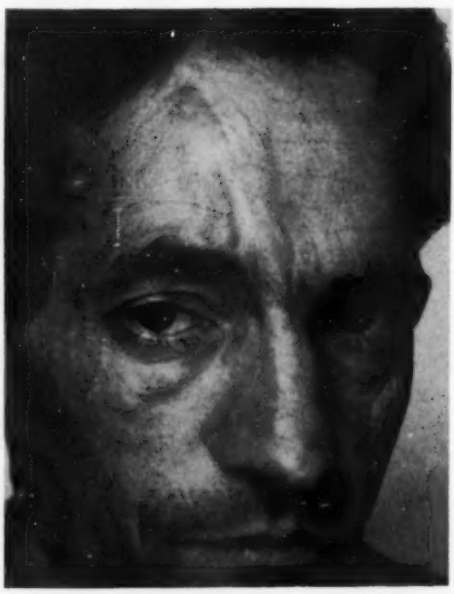

Fig. 2 (Segal, Jablonska and Mrzyglod). Extension of the sclerodermatous focus on the forehead and cheek somewhat off the median line.

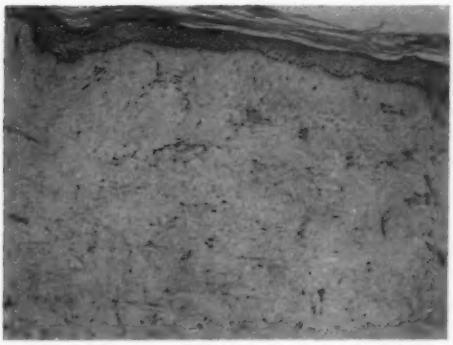

Fig. 3 (Segal, Jablonska and Mrzyglod). Histologic picture of the skin changes (forehead). (Hematoxylin-eosin.) Thinning of the epidermis with flattening of the dermal papillae. Connective tissue in corium compact, sclerosed and homogeneous. Appendages absent. No inflammatory symptoms.

tion where the iris was narrower (figs. 5 and 6). Reaction of the iris to light and convergence was normal. On the anterior capsule of the lens a few dustlike deposits could be seen. The deeper parts of the eye were normal.

LEFT EYE. Vision, 5/4. Tension, 18 mm. Hg. Except for a small group of typical brownish square "stars" on the anterior capsule of the eye, which were the surviving residue of the pupillary membrane, the eye was normal.

Diagnosis. Iritis and sectoral atrophy of the mesodermal layers of the iris of the right eye was diagnosed.

Course of the disease. The patient was given three courses of penicillin treatment at two-month intervals, 3,000,000 units per course. This caused distinct improvement of the skin condition (soften-

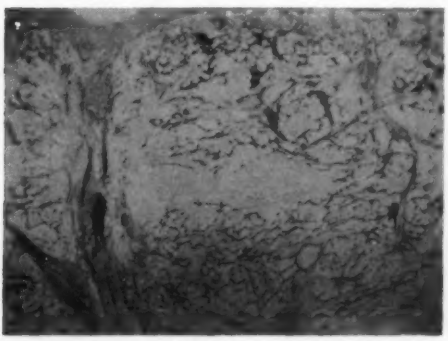

Fig. 4 (Segal, Jablonska and Mrzyglod). Histologic picture of the skin as in Figure 3. (Weigert stain.) Elastic fibers are preserved except in the hyalinized focus in the central part of the corium. In the upper layers of the corium heaped-up elastic tissue (collagen degeneration).

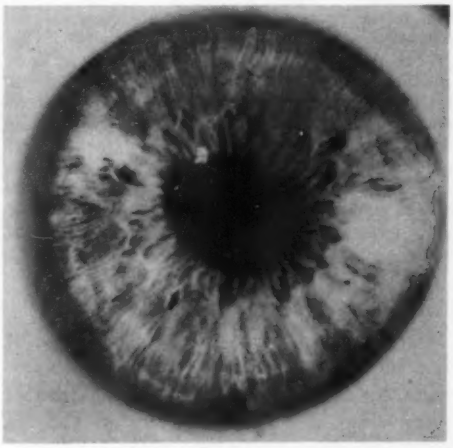

Fig. 5 (Segal, Jablonska and Mrzyglod). Anterior portion of the right eye. In the region of the 9:30-o'clock position, there is noticeable atrophy of distinctly depigmented anterior layers of the iris. The atrophied segment of the iris causes distortion of the pupil, which is somewhat pointed in the direction of the atrophied part (the white spot at the 3:30-o'clock position is an artefact caused by a reflection of the lamp).

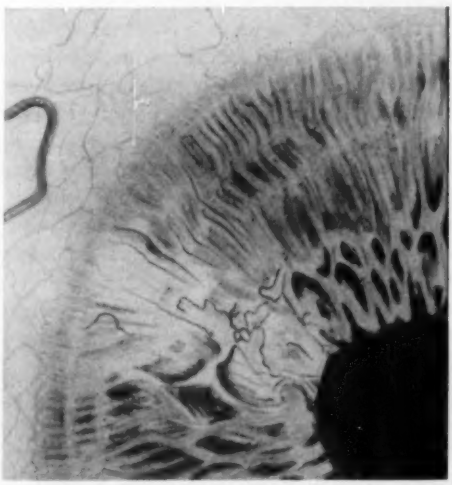

Fig. 6 (Segal, Jablonska and Mrzyglod). Part of the iris affected by sectoral atrophy. Atrophy of trabeculae, depigmentation, and the network of the vessels of the iris visible where trabeculae are atrophied (drawing photographed).

ing of the induration) and disappearance of the lilac ring, which proved lack of activity of the process. Locally, the eye was treated with atropine and Terra-cortril. Inflammatory changes of the iris receded within a few days, the aqueous humor of the anterior chamber became clearer, and the deposits on Descemet's membrane and the lens diminished. After four months, follow-up examination showed traces of the inflammation had disappeared entirely, functional efficiency of the eye was fully restored, and atrophic changes in the iris, as already described, were unaltered.

Discussion

The case described is a typical sabre-cut scleroderma as regards clinical and histologic pictures, as well as chronaximetry. Atrophy within sclerodermatous foci is clearly associated with the principal pathologic process.

Ocular changes, restricted to the side affected by the skin lesions, partly involved the cornea, which showed slightly reduced sensitivity, but mostly the anterior part of the uvea. When the patient called at the clinic we noted iritis, which ran a very inconspicuous course and receded after a few days without leaving any synechias. Deposits on Descemet's membrane were resorbed without trace within a few weeks.

At the same time we noted sectoral atrophy of anterior layers of the iris of the same eye. This change must have been recent because one and one-half years earlier thorough examination at the Lodz Ophthalmological Clinic revealed no changes in the iris. There is the theoretical possibility that the atrophy may have been the result of the inflammation we noted. This, however, seems unlikely. First, the inflammation ran a very mild course and cleared within a few days. Second, except for the segment described, the iris looked normal, its structure was completely normal and it showed neither blurred patterns nor any other features of atrophy, observed occasionally after severe and prolonged uveitis. It is much more likely that the changes were of neurotrophic origin. The morphologic picture warrants no conclusion as to whether these changes are due to lesions of the sympathetic or the parasympathetic (ganglion ciliare) system, but connection with the autonomic nervous system appears certain.

The character of the morphologic changes in scleroderma, that is, indurations, atrophy, hyperpigmentation and depigmentation, loss of hair, disturbed secretion of perspiration and sebum, indicate a neurotrophic background of the disease. Haxthausen's experiments (1947) with skin grafts also support the neurotrophic origin of sclerodermatous foci. John (1949) and Ormea (1955 and 1958) proved in neurohistologic investigations that, in scleroderma, the primary changes are in the autonomic system of the skin and sympathetic ganglia and precede perceptible collagen abnormalities. Thus approached, scleroderma would appear to be a neurovegetative disease and not a collagenosis. This is also confirmed by physiologic investigations, especially of sensory chronaxy which is prolonged in seemingly normal skin, the prolongation also preceding collagen changes.

In linear scleroderma, the connection with the nervous system is particularly conspicuous. The bandlike foci are usually arranged in segments (Vohwinkle, 1929; Rubin, 1948; Korting and Korte, 1958), less rarely along peripheral nerves (Kingery, 1922). This form of scleroderma often appears in younger persons and causes more pronounced atrophies than other varieties. On the face, the subsiding atrophic lesions frequently cause, especially in children, secondary facial hemiatrophy, which occasionally resembles, morphologically, Romberg's idiopathetic hemiatrophy.

The connection between Romberg's idiopathic hemiatrophy and the nervous system is generally known, so that this disease is classified as a neurotrophic disturbance. There is no agreement on the pathogenesis of scleroderma and its connection with the nervous system is not universally admitted. The case referred to, of indisputable scleroderma with ipsilateral neurotrophic changes in the uvea, suggests, we feel, a connection

between scleroderma and the autonomic nervous system.

It is possible that, among the agents causing the condition in our patient, the severe nervous strain which he experienced prior to the appearance of the morbid changes played a role.

Summary

Described is a case of linear scleroderma of the face of the sabre-cut type, with attendant ocular changes consisting of sectoral atrophy of the mesodermal layers of the iris on the side of the skin lesions. The disease developed some months after a grave nervous strain and eye changes appeared within a few months. The nature of the eye changes indicated their neurotrophic origin, suggesting a connection of scleroderma with the nervous system which is especially distinct in linear scleroderma.

We believe linear sabre-cut scleroderma is not identical with Romberg's idiopathic hemiatrophy, although both seem clearly connected with the nervous system.

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References

Archambault, L., and Fromm, N. K.: Progressive facial hemiatrophy. Arch. Neur. & Psychiat., **27**: 529, 1932.

Cassirer, R.: Die Vasomotorisch-trophischen Neurosen. Berlin, Karger, 1912, ed. 2, p. 588.

Cords, R.: Strichförmige Gesichtsatrophie und Auge. Bericht. d. Deutsch. Ophth. Gesell., **47**:53, 1928.

Curtis, A. C., and Jansen, T. G.: The prognosis of localized scleroderma. AMA Arch. Dermat., **78**: 749, 1958.

Dolfus, M.: Un autre cas de sclérodermie en coup de sabre avec lèsions oculaires multiples ayant evolue pendant plus de douze ans. Bull. Soc. belg. Ophtal., **118**:377, 1958.

Franceschetti, A., Jadassohn, W., Paillard, R., Hofer, R., and Golay, M.: Hemiatrophie faciale ou sclerodermie en coup de sabre. Dermatologica, **116**:331, 1958.

Haxthausen, H.: Studies on the pathogenesis of morphea, vitiligo and acrodermatitis atrophicans by means of transplantation experiments. Acta Derm. & Vener., **27**:352, 1947.

Jabłońska, S., Bubnow, B., and Lukasiak, B.: Auswertung von Chronaxiemessungen bei Sklerodermie. Derm. Wschr., **166**:821, 1957-a; Sklerodermieähnliche Zustände: Ihre Differential-diagnose gegenüber Sklerodermie. Derm. Wschr., **136**:1201, 1957-b.

Jabłońska, S., Lukasiak, B., and Bubnow, B.: Zanik połowiczy twarzy i jego związek z twardzina. Pol. Tyg. Lek., R. 13, N. 6, 1958.

John, F.: Arch. Derm. & Syph., **188**:347, 1949.

Josten, K.: Sclerodermie en coup de sabre und Auge. Klin. Monatsbl. f. Augenh., **133**:567, 1958.

Kahler, O.: Ein Fall von beschränkter neurotischer Atrophie im Gesichte. Prager Mediz. Wchschr., **6**:53, 1881. (After Cords.)

Korting, G. W., and Korte, H. E.: Systematisierte circumscripte Sklerodermie, vorwiegend unter dem Bilde eines cervico-thoracalen Quadratensyndroms. Arch. klin. exper. Derm., **207**:499, 1958.

Kingery, L. B.: Scleroderma following nerve injury. Arch. Derm. & Syph., **5**:579, 1922.

Lauber, H.: Ein Fall von Hemiatrophia facialis progressiva mit Beteiligung des Auges. Ztschr. Augenh., **57**:492, 1925.

Marchionini, A.: Dermatologica, **116**:331, 1958.

Meunier, A., and Toussaint, D.: Sclerodermie en coup de sabre avec lesions du fond d'oeil. Bull. Soc. belg. Ophtal., **118**:369, 1958.

Ormea, F.: Zur Pathogenese der diffusen Sklerodermie. Hautarzt, **7**:301, 1952.

———: Sur la pathogenie neuro-végetative de la maladie Sclérodermique. Arch. belg. Derm., **14**:423, 1958.

Osborne, E. D.: Morphea associated with hemiatrophy of the face. Arch. Derm. & Syph., **6**:27, 1922.

Piper, W. N., and Helwig, E. B.: Progressive systemic sclerosis. AMA Arch. Dermat., **72**:535, 1955.

Rubin, L.: Linear scleroderma. Arch. Derm. & Syph., **58**:1, 1948.

Schnyder, U. W.: Circumscripte Sclerodermien mit Weichteil- und Knochenatrophie. Dermatologica, **112**:444, 1956.

Stava, Z.: Zirkumskripte Sklerodermie. Derm. Wschr., **139**:513, 1959.

Vohwinkel, K. H.: Zur pathogenese der Sklerodermie. Arch. f. Derm. & Syph., **158**:28, 1929.

Wartenberg, R.: Progressive facial hemiatrophy. Arch. Neur. & Psychiat., **54**:75, 1945.

Wolff, H. G., and Ehrenclou, A. H.: Trophic disorders of central origin: Report of a case of progressive facial hemiatrophy associated with a lipodystrophy and other metabolic derangements. J.A.M.A., **88**:991, 1927.

DIFFUSION STUDIES WITH OX VITREOUS BODY*

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In recent years the biochemistry of the two unique components of the gel-like vitreous body, the residual protein and the hyaluronic acid, has been elucidated but the mechanism of the interaction between the two components is still not clear. Pirie[1] suggested, from spatial considerations, that the fibrous structure of the residual protein mechanically hindered the free diffusion of hyaluronate molecules. Varga[2] postulated that an occasional covalent bond between residual protein and hyaluronic acid would be sufficient to account for the gel-like structure. Woodin and Boruchoff[3] found in homogenized vitreous bodies an interaction between the two components by viscometric studies. They found evidence of weak coulombic forces acting between the two. We have used the diffusion of pigmented molecules in the vitreous as a technique to investigate this problem further.

METHODS AND MATERIALS

Vitreous preparations. Isolated ox secondary vitreous bodies were obtained in the following manner: An equatorial cut was made through the coats of the eye and the anterior section was separated. The vitreous was then cut away two to three mm. below the ora serrata.

In some eyes cornea and iris were removed to expose the zonular region. In others, a window was cut in the posterior part of the eye to expose an undisturbed area of vitreous calculated to be equal in area to that of the annular ring.

Diffusion chamber. A leucite box 2.0 cm. wide, 4.0 cm. long and 4.0 cm. high was separated into two parts by a crosswise divider 1.0 cm. from one end. The divider had a hole in the center over which a piece of wide mesh nylon fabric was cemented. An isolated vitreous body was placed in the larger section and vitreous filtrate with added pigment in the smaller part. The chamber fitted into a special carrier to adapt it for use in a colorimeter. The mesh provided a sharp boundary for observation of pigment diffusion into the vitreous.

Pigment preparations. Hemoglobin was prepared from fresh heparinized ox blood. The red cells were washed thoroughly with isotonic saline, and were then laked in distilled water. Cell debris was removed by centrifugation and the hemoglobin was precipitated by 45-percent saturation with ammonium sulfate. The precipitated hemoglobin was taken up in distilled water and dialysed in water until free of ammonium sulfate.

Hemocyanin was prepared from fluid withdrawn from the hemoceles of the California garden snail.[4] The hemocyanin containing fluid was diluted with an acetate buffer (pH 5.4 in 0.9-percent NaCl) to a total salt concentration of about 0.1 percent[5] and centrifuged four hours at 0°C. at 100,000 × G. The blue pigment collected as a solid gelatinous pellet which could be separated from a lighter overlay of yellow mucus.

Horse liver ferritin was donated.# For use, the pigment solutions were added to fresh vitreous filtrate in amount sufficient to give a strong color.

Dialysis membranes. One-inch diameter filters having pore diameters 450 mμ,* 50 mμ,* and 5.0 mμ† were used to cap leucite

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Courtesy of Dr. R. A. Fineberg, Department of Biochemistry, University of California Medical School, San Francisco.

* Millipore Filter Corp., Bedford, Massachusetts.

† Nalfilm D-30, sample from National Aluminate

TABLE 1

PIGMENT DIFFUSION INTO ISOLATED VITREOUS

Compound	Approximate Size (mμ)	Ratio of Size	Diffusion Rate (mm./24 hr. 20°C.)	Ratio of Rates
Hemoglobin	5.5	1	3.5–4	1.0
Ferritin	11.0	2	1.5–2	0.5
Hemocyanin	22.0	4	0.75–1.25	0.25

chambers of 5.0 ml. capacity filled with vitreous filtrate. Standard dialysing tubing‡ of specified pore diameter of about 5.0 mμ was used.

Viscosity measurements. Relative viscosity ($N_{vit.filt.}/N_{water}$) was measured in Ostwald viscometers of 5.0 ml. capacity at 37°C.

Hyaluronic acid determination. Hyaluronic acid was estimated by measurement of its glucuronic acid following dialysis of the solutions in isotonic saline using the carbazole method.[6]

Hyaluronidase§ was used at a level of 100 TRU/ml., diluted in acetate buffer pH 5.4 in isotonic saline.

RESULTS AND DISCUSSION

DIFFUSION OF LARGE MOLECULES INTO ISOLATED VITREOUS

Comparative rates were measured for the diffusion of the pigments into freshly isolated, unoriented vitreous bodies. In the diffusion chamber procedure, under uniform conditions, rates were dependent only upon the size of the diffusing molecules. Table 1 shows the results of this work.

Hemoglobin has been reported to have the shape either of a sphere[7] or a cylinder of small axial ratio.[8] Ferritin shows a nearly spherical shape in electron micrographs.[9] Hemocyanin may be a cylinder 89 mμ long by about 22 mμ diameter, but in the presence of salts it may dissociate into halves or quarters along its long axis yielding a cube about 22 mμ on a side.[10] It is apparent from our data that we have used the shorter molecule.

Within the limits of accuracy of the observations, the diffusion rates of the large molecules are inversely proportional to their sizes. The rate observed for hemoglobin is in agreement with that of von Sallmann.[11] No structural barrier to diffusion was observed even for the largest molecules in these vitreous preparations.

DIFFUSION OF LARGE MOLECULES INTO INTACT VITREOUS

The permeability to hemoglobin of the vitreous surface at specific sites was next studied (table 2). In the isolated vitreous preparation orientation was lost and surface areas were disturbed. Here, the zonular ring and posterior vitreous areas were carefully exposed in situ to pigment in vitreous filtrate and, for comparison, the same solution was injected equatorially into the center of the vitreous of other eyes. Some of the eyes with exposed annular ring were pretreated with hyaluronidase.

Basic fuchsin is a dye of low molecular weight relative to that of the protein molecules and it was used here as an indicator of the rate of diffusion of a small molecule. Within the vitreous and at the peripheral window, fuchsin diffused rapidly. Hemoglobin was slowed in penetrating the posterior vitreous surface in comparison to the distance it traveled within the vitreous, 2.0 mm. versus 3.0 mm. in 24 hours. This difference of rates may be within experimental error due to difficulty of exact observation.

The vitreous at the annular ring is dif-

Corp., Chicago 38, Illinois.

‡ Visking Corp., Chicago 38, Illinois.

§ Courtesy Wyeth Institute for Medical Research, Philadelphia, Pennsylvania.

TABLE 2

PIGMENT DIFFUSION INTO INTACT VITREOUS
(mm./24 hr. 20°C.)

Pigment	Peripheral Vitreous Window	Within Vitreous	Annular Ring
Basic fuchsin	Nearly fills vitreous	Fills vitreous	About 5 mm.
Hemoglobin	About 2 mm.	3 mm. radius of cylinder along needle axis	On surface at ora serrata
Hb after H-Ase	—	—	About 6 mm.

ferent from the secondary vitreous; it is composed of tertiary vitreous containing the zonular fibers and possesses an anterior limiting layer which is a condensation of primary and secondary vitreous elements. The rate of diffusion of basic fuchsin was slower through this surface than elsewhere. This area was not penetrated by hemoglobin until hyaluronic acid was removed, showing that hyaluronic acid in the fibrous structure presents a barrier to protein diffusion, as suggested by Pirie and van Heyningen.[13]

Some of the eyes diffused with hemoglobin were examined for pattern of pigment distribution. No color was apparent in the retrolental vitreous. The pigment traveled to the posterior along the vitreous surface beyond the ora serrata where surface permeability was high enough for it to diffuse inward.

DIFFUSION OF PIGMENTS AND HYALURONIC ACID FROM ISOLATED VITREOUS BODIES

Since diffusion of ferritin was not hindered in the isolated vitreous, we desired to see if the same would hold true for hyaluronic acid. Hyaluronic acid has been estimated to have a molecular weight of from 340,000[13] to 1,000,000.[14] The molecular weight of ferritin is of the same order, about 750,000.[9] A direct comparison was made of the rates at which each compound left isolated vitreous bodies. Some vitreous preparations were saturated with ferritin by soaking them in a solution of ferritin in vitreous filtrate for three weeks. These and freshly isolated vitreous bodies were separately self-dialysed in frequent changes of water. At intervals the amount of ferritin remaining was measured by color at 420 mμ and in the other group the remaining hyaluronic acid was analyzed in the filtrates from the vitreous bodies removed at different times. Remaining hyaluronic acid was also measured in a second group of vitreous bodies dialysed in isotonic saline solution, and the rates were no faster than for the group dialysed in water. The degree of polymerization of vitreous hyaluronate is known to be somewhat altered in the presence of salts. We have found that dialysis of vitreous filtrate against distilled water doubles its relative viscosity. Here, even in the presence of salts, hyaluronic acid diffusion was not accelerated. Figure 1 shows the results of these experiments.

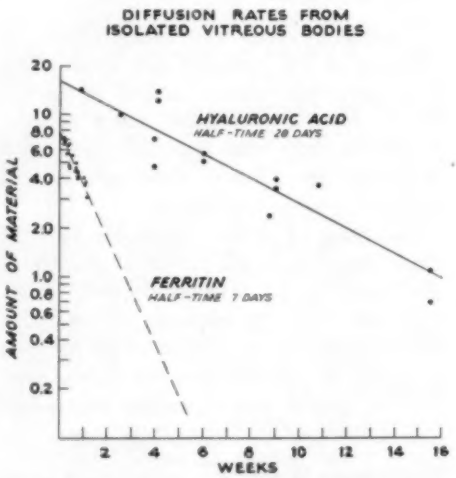

Fig. 1 (Suran and McEwen). Diffusion rates from isolated vitreous bodies.

The amounts of material remaining in the vitreous are plotted on a logarithmic scale against time on a linear scale. Hyaluronic acid has a half-time of 28 days (every 28 days one-half of the hyaluronic acid in the soaking vitreous washes out) and ferritin an average half-time of about seven days. These data indicate that the diffusion of hyaluronic acid as compared to ferritin on a molecular weight basis is considerably hindered.

Diffusion of hyaluronic acid through membranes

Pirie[1] found, using a mucin clot test, that only disaggregated hyaluronic acid dialysed into the wash fluid during prolonged washing of vitreous bodies, while aggregated hyaluronate remained within. She suggested that a disaggregating system, possibly copper-ascorbic acid, was present. The possibility of the presence of a small amount of hyaluronidase should also be considered.[14] Takagi[15] found a dialysable thermostable disaggregating system in the vitreous. However, in our experience vitreous filtrate if kept refrigerated and free of contamination, is quite stable over long periods of time (no change in viscosity).

An experiment was devised to investigate possible disaggregation of dialysing vitreous filtrate. Fresh, pooled vitreous filtrate in tubing was dialysed for about three months in saline at 0°C. and sampled at intervals. No significant volume change occurred. The concentration of hyaluronic acid remained unchanged indicating that fragmentation to dialysable size had not occurred. A reduction in viscosity from 1.81 to a constant level at 1.41 occurred, with a half-time of 21 days. Since this time is appreciably slower than the diffusion time of hyaluronic acid, it is probably not rate determining. A control aliquot of the same solution kept in glass maintained under similar conditions showed no such viscosity change. The dialysis was repeated for seven weeks with sized membranes the same and of greater pore size than the tubing. Again, no changes in concentration were found. The viscosities of the solutions ranged from 1.41 to 1.75. Hyaluronic acid can just be filtered under pressure through pores of size 230 mμ,[3] so that one might expect fragments to diffuse easily through 450 mμ holes.

These experiments indicate that the diffusion of hyaluronic acid into or from the vitreous is not limited by the rate of fragmentation to dialyzable size. The slight drop in viscosity found in these experiments is probably a reflection of the reduction of the polydispersity of hyaluronic acid to a more uniform size distribution. The mucin clot test is sensitive to the largest aggregates, as the loss of clotting is the first sign of disaggregation by hyaluronidase.

If we assume that the hyaluronic acid molecule exists in the unhydrated state in the vitreous humor it would have a diameter similar to that of ferritin and should have a comparable diffusion rate, but it is found to have a diffusion rate approximately four times slower than ferritin. Hyaluronic acid probably exists in solution as a hydrated random coil molecule.[16] The simplest assumption which might be made is that the diffusion rate of hyaluronic acid from isolated vitreous bodies is the result of free diffusion of hydrated hyaluronic acid with an effective diameter about four times that of ferritin.

The relation between the diameter of a molecule and its degree of hydration is given by the formula:

$$(D \times 10^{-7})^3 = \frac{6WM}{\pi A}$$

where:

D = diameter of molecule in mμ
W = hydration in ml./gm. of dry weight of hyaluronic acid
M = mol. wt. hyaluronic acid = 10^6 gm./mol.
A = Avogadro's number = 6×10^{23} molecules/mol.

Several investigators have estimated either the size or the amount of hydration of hyaluronic acid. These values are given in Table 3 and the corresponding values have been calculated from the above formula. The

TABLE 3

RELATION OF DIAMETER TO HYDRATION OF HYALURONIC ACID

Diameter (mμ)	Hydration (ml./gm.)	Reference
34	12*	17
44	27	
66	90	3
86–117	200–500	16
~200	~760	Maximum hydration

* Underlined value is value cited in reference.

final value in the table (760 ml./gm.) is calculated on the basis of maximum possible hydration, 10 ml. of water/4.2 mg. of dry weight of hyaluronic acid in a beef secondary vitreous.

It may be seen from Table 3 that the value of 44 mμ diameter which would account for the free diffusion of hyaluronic acid being four times slower than ferritin fits in quite well for a molecule with moderate hydration. Twelve ml./gm. given by Blumberg and Ogsten[17] is the minimum amount of hydration which would exclude the interpenetration of an albumin molecule into the hydrated hyaluronic acid. The value of 66 mμ is calculated by Woodin and Boruchoff[3] from their physical chemical data. The data obtained from our diffusion studies indicate that hyaluronic acid is more hydrated than Blumberg and Ogsten[17] assume.

The consequence of the assumption of free diffusion is that there is no need to postulate interaction between hyaluronic acid and residual protein in the vitreous structure. The weak coulombic forces between hyaluronic acid and residual protein found by Woodin and Boruchoff[3] may exist. If the rupture of these forces is rate determining, then the hyaluronic acid molecule is less hydrated than their calculations would indicate. For hyaluronic acid to be hydrated sufficiently to account for the observed rate of diffusion, the breaking of the bonding forces would not be rate determining. Self-dialysis of vitreous bodies in isotonic saline, which process might be expected to break such bonds more easily than self-dialysis in distilled water, did not show an increased rate of diffusion. Hyaluronic acid, even at maximum hydration (200 mμ diameter), should diffuse through a membrane with 450 mμ diameter pores if unrestricted. It appears in this case that bonding forces are between the hyaluronic acid and the plastic membrane.

SUMMARY

1. Large colored protein molecules diffuse freely in the vitreous body at rates inversely proportional to their molecular weights.

2. From diffusion studies it is concluded that hyaluronic acid is a moderately hydrated molecule and that it diffuses freely from isolated beef secondary vitreous bodies.

3. The rate of diffusion of hyaluronic acid is not limited by rates of disaggregation or bond rupture.

4. The zonular region of the vitreous is a barrier to the diffusion of small protein molecules.

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REFERENCES

1. Pirie, A.: Ox vitreous humor: 2. Hyaluronic acid relationships. Brit. J. Ophth., **33**:271, 1949.

2. Varga, L.: Physico-chemical properties of the vitreous. XVII Internat. Cong. Ophth., 1954, Pt. II, p. 1025.

3. Woodin, A. M., and Boruchoff, S. A.: Particle interaction of solutions derived from ox vitreous humor. J. Biophys. & Biochem. Cytol., **1**:489, 1955.

4. Williams, R. C., and Wycoff, R. W. G.: Electron shadow-micrographs of hemocyanin molecules. Nature, **156**:68, 1945.

5. Brohult, S.: Hemocyanin of helix pomatia. Chem. Zentralbl., 665 (1942, II). Cited in Chem. Absts., **37**:5092, 1943.

6. Dische, Z.: Methods in Biochemistry. New York, Interscience, 1955, v. 2, p. 313.

7. deRobertis, E., Franchi, C. M., and Podolsky, M.: Aerosol technique for the study of macromolecules with the electron microscope. Biochem. & Biophys. Acta, **11**:507, 1953.

8. Bragg, W. L.: X-ray analysis of hemoglobin. Proc. Roy. Soc. (London) Series B, **141**:67, 1953.
9. Harrison, P. A.: Structures of ferritin and apoferritin: Some preliminary studies. J. Molecular Biol., **1**:69, 1959.
10. Schramm, G., and Berger, G.: Electron microscopic investigations of the structure of hemocyanin of helix pomatia. Z. Naturforch, **7B**:284, 1952.
11. von Sallmann, L.: Experimental studies on the vitreous. 1. Experiments on diffusion in the vitreous and on permeability of its surface condensation layer. AMA Arch. Ophth., **42**:583, 1949.
12. Pirie, A., and van Heyningen, R.: Biochemistry of the Eye. Springfield, Ill., Thomas, 1956, p. 252.
13. Laurent, T. C.: Studies on hyaluronic acid in the vitreous body. J. Biol. Chem., **216**:263, 1955.
14. Brunish, R., Rowan, J. W., and Irvine, S. R.: Proteins and hyaluronic acid of beef vitreous humor. Tr. Am. Ophth. Soc., **52**:369, 1954.
15. Tagaki, Y.: The viscosity reducing substance of hyaluronic acid in the vitreous body. Folia Ophthal. Japan, **7**:1, 1956. Cited in Ophthalmic Lit., **10**:736, 1956.
16. Blumberg, B. S., and Ogston, A. G.: Physiochemical studies on hyaluronic acids. In Ciba Foundation Symposium on the Chemistry and Biology of Mucopolysaccharides. (Wolstenholme, G. E. W. and O'Connor, M., eds.) London, Churchill, 1958, pp. 22-41.
17. ———: The selective solvation of the hyaluronic acid complex of ox synovial fluid. Biochem. J., **63**:715-717, 1956.
18. Bembridge, B. A., Crawford, G. N. C., and Pirie, A.: Phase contrast microscopy of the animal vitreous body. Brit. J. Ophth., **36**:131, 1952.
19. Balazs, E. A.: Structure of the vitreous gel. XVII Internat. Cong. Ophth., 1954, Pt. II, p. 1019.

RESISTANT STAPHYLOCOCCUS CONJUNCTIVITIS

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Since the study on the effects of the eye-patch on the organisms of the conjunctival sac was reported by me[1] in 1950, many of the same bacteria have become resistant pathogens to treatment, or possibly some new type of bacterial infection has occurred in the conjunctiva. In 1950, the commonest organisms found in the grossly normal conjunctiva were Staphylococcus albus and Staphylococcus aureus. Mindful that the processes affecting the conjunctiva have three avenues of approach: (1) exogenous, (2) endogenus and (3) by local disease, the following procedure was set up on a series of cases in 1959. The objective was to find the cause and the response to treatment of resistant types of conjunctivitis.

PROCEDURE FOLLOWED

Patients with conjunctivitis that did not respond to two different kinds of antibiotics were sent to a well-qualified laboratory, after receiving no local treatment for five days, for smears and cultures of the conjunctiva plus sensitivity tests. The tests were all done in the early morning because bacteria are more likely to be found in the conjunctival sac at this time. Scraping with a previously flamed platinum loop is recommended because otherwise bacteria found under the surface cells may not be found. Getting below the surface cells is very important because many laboratories report negative growths of bacteria when a more thorough investigation would have given a positive bacterial growth. Table 1 shows the laboratory findings and the first drug used, successive drugs that were used and the end-results. Smear studies with gram-stain were done both from direct smears from the conjunctiva and from the colonies of the bacteria grown on the agar plates. Fungus studies were done if no bacteria were found and if the case responded unusually to antibiotic therapy.

From Table 1, it can readily be seen that the most common resistant bacteria was Staphylococcus aureus. The second most common

TABLE 1

LABORATORY RESULTS AND RESPONSES TO DRUGS IN 41 CASES OF CONJUNCTIVITIS

Diagnosis	Smear, O.S.	Culture, O.S. Broth	Culture, O.S. BAP	Smear, O.D.	Culture, O.D. Broth	Culture, O.D. BAP
Recurrent conjunctivitis, meibomianitis & keratitis	Occas. epith. cell, occas. poly, no eosin or bacteria	Pure G+cocci like Staph.	Pure hemolytic Staph. aureus	Occas. epith. cell, no polys, eosins or bacteria	Sterile	Sterile
Conjunctivitis	Occas. epith. cell, masses of polys, no eosin or bacteria	Pure G+cocci like Staph.	Pure hemolytic Staph. aureus	Occas. epith. cell, & poly, no eosin or bacteria	Pure G+cocci like Staph.	Pure hemolytic Staph. aureus
Keratitis	Occas. epith. cell, no polys, eosin or bacteria	Scant growth G +cocci like Staph.	Pure hemolytic Staph. aureus	Occas. epith. cell, occas. poly, no eosin or bacteria	Pure G+cocci like Staph.	Sterile
Chronic conjunctivitis & keratitis	Occas. poly, few lympho, occas. epith. Rare eosin, no bact. or inclusions	Pure G+cocci like Staph.	Pure hemolytic Staph. aureus	Mod. number of polys lymph & eosin, few epith, no bacteria or inclusions	Pure G+cocci like Staph.	Pure hemolytic Staph. aureus
Blepharitis	Occas. epith. cell, no polys, no eosin or bacteria	Pure G+cocci like Staph.	Pure hemolytic Staph. aureus	Occas. epith. cell, few polys, no eosin or bacteria	Pure G+cocci like Staph.	Pure hemolytic Staph. aureus
Conjunctivitis	Rare epith. cell, no polys, eosin or bacteria	Pure G+cocci like Staph.	Pure hemolytic Staph. aureus	Rare epith. cell, no polys, eosin or bacteria	Pure G+cocci like Staph.	Pure hemolytic Staph. aureus
Recurrent conjunctivitis	Few epith. cell. no polys, eosin or bacteria	Pure G+cocci like Staph.	Pure hemolytic Staph. aureus	Few epith. cell, no polys, eosin or bacteria	Pure G+cocci like Staph.	Pure hemolytic Staph. aureus
Conjunctivitis, O.D.				Few epith. cells, no polys, eosin or bacteria	Pure G+cocci like Staph.	Pure hemolytic Staph. aureus
Conjunctivitis, O.S.	Rare epith. cell, no polys, eosin, or bacteria	Pure G+cocci like Staph.	Pure hemolytic Staph. aureus			
Conjunctivitis, O.S.	Few epith. cells, no polys, eosin or bacteria	Gram neg. bacilli Occas. G+ cocci-like Staph.	Hemolytic G+bacilli			
Mild keratitis	Few epith. cells, no polys, eosin, or bacteria	Pure G+cocci like Staph.	Pure hemolytic Staph. aureus	Many epith. cells, no polys, eosins or bacteria	Pure G+cocci like Staph.	Pure hemolytic Staph. aureus
Keratitis	Occas. epith. cell, no polys, eosin or bacteria	Sterile	Sterile	Many epith. cell, no polys, eosin or bacteria	Pure G+cocci like Staph.	Pure hemolytic Staph. aureus
Conjunctivitis	Epith. cells, few polys, no eosins, or bacteria	Pure G+cocci like Staph.	Pure hemolytic Staph. aureus	Occas. epith cell, few polys, no eosins or bact.	Pure G+cocci like Staph.	Pure hemolytic Staph. aureus
Conjunctivitis	Protein precipitate, no cells, bacteria	Pure G+cocci like Staph.	Pure hemolytic Staph. aureus	Protein precipitate, no cells, no bact.	Pure G+cocci like Staph.	Pure hemolytic Staph. aureus
Blepharoconjunctivitis	Rare epith. cell, no polys, eosin, or bacteria	Pure G+cocci like Staph.	Pure hemolytic Staph. aureus	Rare epith. cell, no polys, eosin, or bacteria	Pure G+cocci like Staph.	Pure hemolytic Staph. aureus
Blepharitis	Occas. epith. cell, no polys, eosin or bacteria	Pure G+cocci like Staph.	Hemolytic Staph. aureus	Few epith. cells, no polys, eosin, or bacteria	Pure G+cocci like Staph.	Hemolytic Staph aureus
Keratitis	Rare epith. cell, no polys, eosin or bacteria	G+cocci like Staph.	Growth of Ps. aeruginosa and hemolytic Staph. aureus	Rare epith. cell, no polys, eosin, or bacteria	G+cocci like Staph. and occas. G+bacilli	Growth of Ps. aeruginosa and hemolytic Staph. aureus
Blepharitis	Occas. epith cell, rare poly, no eosin or bacteria	Pure G+cocci like Staph.	Hemolytic Staph. aureus	Occas. epith. cell, rare poly, no eosin or bacteria	G+cocci like Staph. and Strep.	Hemolytic Staph aureus.
Keratitis, O.U.	Rare epith. cell, no polys, eosin or bacteria	Pure G+cocci like Staph.	Pure hemolytic Staph. aureus	Occas. epith. cell, no polys, eosin or bacteria	Pure G+cocci like Staph.	Pure hemolytic Staph. aureus
Conjunctivitis	Squamous cell, no leukocytes or bacteria	Pure G+cocci like Staph.	Pure hemolytic Staph. aureus	Protein precipitate, no cells or bacteria	Pure G+cocci like Staph.	Pure hemolytic Staph. aureus
Blepharitis	Occas. epith cell, rare poly, no eosin or bacteria	Pure G+cocci like Staph.	Pure hemolytic Staph. aureus			
Keratitis	Occa. epith. cell, no polys, eosin or bacteria	Pure G+cocci like Staph.	Hemolytic Staph. aureus	Rare epith. cell, no polys, eosin, or bacteria	Pure G+cocci like Staph.	Hemolytic Staph aureus
Follicular conjunctivitis	Occas. epith. cell. no polys, eosin, or bacteria	Pure G+cocci like Staph.	Pure hemolytic Staph. aureus	Epith. cells, no polys, eosin, or bacteria		
Blepharitis	Occas. epith. cell, few polys, no eosin or bacteria	Pure G—cocci like Staph.	Pure hemolytic Staph. aureus	Occas. epith. cell, no polys, eosin or bacteria	Pure G+cocci like Staph.	Pure hemolytic Staph. aureus
Conjunctivitis (recurrent)	Rare epith. cell, no polys, eosin or bacteria	Pure G+cocci like Staph.	Pure hemolytic Staph. aureus	Rare epith. cell, no polys, eosin or bacteria	Pure G+cocci like Staph.	Pure hemolytic Staph. aureus
Keratitis, O.U.	Occas. epith. cell, no polys, eosin or bacteria	Pure G+cocci like Staph.	Pure hemolytic Staph. aureus	Occas. epith. cell, no polys, eosin or bacteria	Pure G+cocci like Staph.	Pure hemolytic Staph. aureus

Chloromycetin	Novobiocin	Ilosone	Erythromycin	Penicillin	Streptomycin	Sulfadiazine	Tetracycline	Terramycin	Gantrisin	Furacin	Aureomycin	Drug Used	Response	Drug Used	Response
S		S	S	S	S	R	S	S	R	S	S	Chloromycetin	Poor	Furacin	Fair response 1 wk.
S	S		S	S	S	R	S	S		S	S	Chloromycetin	Good response 4 da.		
S	S	S	S	S	S	R	S	S	R	S	S	Furacin	Poor response 1 wk.		
S			S	R				R	R	R	R	Chloromycetin	Fair response 2 da. & 10 da.		
S	S		S	S	S	R	S	S	R	S	S	Aureomycin	Good response 2 wk.		
R	S	S	S	ss	ss	R	S	S	R		S	Erythromycin	Good response 2 wk.		
S			S	S	S		S	S	S		S	Penicillin	Fair response 2 wk.	Neosporin	Good response 2 wk.
S	S	S		S	ss	R	S	S	R	S	S	Penicillin	Response 8 da.		
S			S	S	S	S	S	S	R		S	Erythromycin	Good response 3 wk.		
S				R	S	R	S	S	R		S	Erythromycin	Fair response		
S				S	S	S	S	S	S	S	S	Penicillin	Response 3 wk.		
R	S	S	S	S	R	R	R	R	R	S	R	Penicillin	Poor response	Furacin	Good response 26 da.
S		S	S	R	S		R	R	R	S	R	Chloromycetin	Fair response 7 da.		
R	S	S	S	R	R	S	S	S	R	S	S	Penicillin	Good response but allergic to penicillin	Neomycin	Good response 1 wk.
S			S	S	R		S	R	R	S	S	Aureomycin	Good response 4 da.		
S	S	S	S	S	R	R	R	R	R	S		Erythromycin	Good response 5 da.		
S	S		S	S	S	R	S		R	S	S	Penicillin	Good response 28 da.		
S	S			S	S	R	S	S	R		S	Aureomycin	Good response		
R		S	S	S	S		S	S	R	S	S	Penicillin	Moderate response 1 wk.		
R	S	S	S	ss	ss	R	R	R	R	S	R	Furacin	Marked improvement 9 da.		
S		S	S	S	S	R	S	S	S	S	S	Chloromycetin	Good response 1 wk.		
S		S	S	S	S	R		S	R	S	S	Furacin	Response in 3 da. but recurred		
s	S	S	S	S	R	R	R	R	R	S	R	Chloromycetin	Responded in 1½ wk.		
R	S	S	S	ss	R	R	R	R	R		R	Penicillin	Excellent response 7 da.		
S	S	S	S	R	S	R	R	R	R	S	R	Chloromycetin	Fair response 9 da.		
s	ss	S	S	S	S	R	S	S	R		S	Chloromycetin	Poor response		

TABLE 1—*Continued*

Diagnosis	Smear, O.S.	Culture, O.S. Broth	Culture, O.S. BAP	Smear, O.D.	Culture, O.D. Broth	Culture, O.D. BAP
Conjunctivitis	Many epith. cells, rare poly, no bact. or eosin	Sterile	Sterile	Mod. number of epith. cells, occas. poly, no bacteria or eosin	Pure G+cocci like Staph.	Pure hemolytic Staph. aureus
Conjunctivitis	Many epithelial cells, mod. no. of polys, no eosin or bact.	Pure G+cocci like Staph.	Pure hemolytic Staph. aureus	Rare epith. cell, no polys, eosin or bacteria	Pure G+cocci like Staph.	Pure hemolytic Staph. aureus
Keratitis each cornea nasally	Rare epith. cell, no polys, eosin, or bacteria	Sterile	Sterile	Occas. epith. cell, no polys, eosin or bacteria	Pure G+cocci like Staph.	Scanty growth of Staph. aureus
Keratitis, corneal erosions (diabetic)	Occas. epith. cell, rare poly, no eosin or bacteria	Pure G+cocci like Staph.	Pure hemolytic Staph. aureus	Occas. epith. cell, no polys, eosin or bacteria	Pure G+cocci like Staph.	Pure hemolytic Staph. aureus
Follicular conjunctivitis	No WBC's found, rare epith. cell, no bacteria	Pure G+cocci like Staph.	Pure hemolytic Staph. aureus	Occas. lymph. rare epith. cell, no polys, bacteria or eosinophils	G+cocci and short G+bacilli like diptheroids	No growth in 24 hr.
Keratitis				Many epith. cells, few polys, no eosin, no bacteria	G+cocci like Staph.	Staph. albus
Blepharo conjunctivitis	Mod. no. epith. cells, no polys, eosin or bacteria	Pure G+cocci like Staph.	Pure hemolytic Staph. aureus	Few epith. cells, no polys, eosin or bcteria	Pure G+cocci like Staph.	Pure hemolytic Staph. aureus
Follicular conjunctivitis	Scattered degenerated epith. cells, occas. poly, no bact. eosin or inclusions	Pure G+cocci like Staph.	Pure hemolytic Staph. aureus	Mod. no. of degen. epith. cells, no leuk. eosin. bact. incls.	Pure G+cocci like Staph.	Pure hemolytic Staph. aureus
Conjunctivitis	Few epith. cells, no polys, eosin or bacteria	Sterile	Sterile	Many epith. cells, mod. number of polys, no eosin or bacteria	Sterile	Sterile
Conjunctivitis	Few degenerated cells, occas. recognizable poly, no bacteria	Sterile	Sterile	Small amount of debris, no cells or bacteria	No growth in 48 hr.	No growth in 48 hr.
Conjunctivitis and meibomianitis				Rare epith. cell, no polys, eosin bact. or inclusions	G+cocci like Staph.	Hemolytic Staph. aureus
Conjunctivitis	Occas. epith. cell, no polys, eosin or bacteria	Pure growth of G + cocci	Pure hemolytic Staph. aureus	Occas. epith. cell, no polys, eosin or bacteria	Pure G+cocci	Pure hemolytic Staph. aureus
Blepharitis	Occas. epith. cell, no polys, eosin or bacteria	Pure growth of G + cocci	Pure hemolytic Staph aureus	Occas. epith. cell, no polys, eosin or bacteria	Pure G+ cocci	Hemolytic Staph. aureus
Conjunctivitis		Pure G+cocci like Staph.	Pure hemolytic Staph. aureus		Pure G+cocci like Staph.	Pure hemolytic Staph. aureus
Superficial keratitis	Rare leukocyte, rare G+ micrococci	Pure G+cocci like Staph.	Pure hemolytic Staph. aureus Mannitol pos. Coagulase pos.	Absence of cells. Rare G+ micrococci	Pure G+ cocci	Hemolytic Staph. albus

was Staphylococcus albus. The drug which gave the best result was penicillin and the second best drug was Chloromycetin.

Penicillin was used in solution (1000 units /cc.) rather than ointment because some ointments appear to have lost their strength. Penicillin in solution keeps from seven to 14 days when refrigerated. It is evident that, since penicillin is not used as readily as it was years ago, this drug is again effective against gram-positive infections that a number of broad-spectrum antibiotics will not touch. Chloromycetin solution, which is stable for 10 days at room temperature, has been a consistently good drug for many types of conjunctivitis.

Neomycin which I have found to work well against both gram-positive and gram-negative organisms[2] was not as effective as was expected. This drug also appears to give a number of local allergic responses when it is used in the usual conjunctivitis cases seen in the office practice. Sorsby feels that the neomycin not only has a great range and is

												Drug Used	Response	Drug Used	Response
R	S		S	S	S	R	S	S		S	R	No antibiotic used	Adrenalin; eye quiet		
S	S	S	S	S	R	R	R	R	R	S	S	Penicillin			
S			S	S	S	S		S	O		S	Chloromycetin	Poor response	Penicillin	Good response 28 da.
ss	S	S	S	R	R	R	R	R	S	S	S	Furacin	50% improved	Erythromycin	75% improved 32 da.
S			S	S				S	R	S	S	Furacin neo-hydeltrasal	Poor response	Penicillin	Poor response
S		S	S	S	S	S	R	S	S	S	S	Neosporin	Poor response		
S			S	S	S			S	R		S	Achromycin	Good response 1 wk.		
S			S	S				S	R	S	S	Penicillin	Poor response	Erythromycin	Poor response
												Metreton	Good 1 wk.		
												Negative	No drug given		
S			S	S				S	R		S	Aureomycin	Good 1 wk.		
S		S	S	S	R	R	S		R	S	S				
ss	S	S	S	S	ss	R	S	S	R	S	S	Sulfa	Good 2 wk.		
R	S	S	S	S	S	R	R	R	R		R	Penicillin	Good response		
S	S	S	S	S	S	R	S	S	R	S		Penicillin	Good 4 da.		

suitable for subconjunctival injection but may also be the antibiotic of choice when the casual organism is unknown.

Furacin eye solution, which has a bacteriostatic and bacteriophagic effect, makes the epithelium more compact and has a soothing and antitransudative effect.[3] Furacin is another drug which had fallen into partial disuse but which is again used against resistant bacteria.

Another drug is erythromycin which comes only as an ointment for local use in the eye and is well known to be effective against gram-positive organisms, such as Staphylococcus and Streptococcus.

As this series of patients shows the answer for treatment of resistant bacteria of the conjunctiva has not been completely found. Possibly the new drugs, novobiocin and spiromycin[4] may help solve the problem. The presence of antibiotic-producing bacteria in the healthy eye leads one to speculate as to their protective value against pathogens. Halbert, et al.[5] have shown that many strains of

Staphylococcus from normal flora of the eye are able to produce antibiotics. It might be possible to introduce an easily treated bacteria onto animal corneas or conjunctivas resistant to treatment in animals to learn if the resistant bacteria could be controlled. This same experiment might be tried to heal recurrent breakdowns of the cornea so that a healthy scar would be produced.

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References

1. Linhart, R. W.: Am. J. Ophth., **33**:1280, 1950.
2. Sorsby, A., and Ungar, U.: Neomycin in ophthalmology. Ann. Roy. Coll. Surgeons England, **22**: 107, 1958.
3. Bulands, M.: Application of furacin in ophthalmology. Klin. oczna, **28**:139, 1958.
4. Sery, T. W., Paul, S. D., and Leopold, I. H.: Novobiocin, a new antibiotic. Ocular penetration and tolerance of a new antibiotic; Spiromycin. Antibiotics Ann., 1958-1959.
5. Halbert, S. P., Kazar, C. S., and Sivick, L. S.: Mixed bacterial infections in relation to antibiotic activities. AMA Arch. Ophth., **57**:716, 1957.

OPHTHALMOLOGIC EXPERIENCES WITH A NEW VASOCONSTRICTOR AND A NEW ANTI-INFLAMMATORY AGENT*

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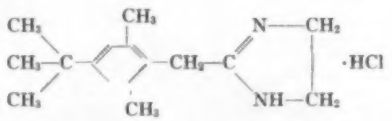
Various combinations of antibiotics with vasoconstrictors and steroids have been introduced into the armamentarium of the ophthalmologist and some of them have gained wide acceptance. Some time ago a pharmaceutical manufacturer† suggested a study on two of their products: one a vasoconstrictor and the other an anti-inflammatory agent combined with neomycin and the same vasoconstrictor.

The following information was supplied by the manufacturer: "Among the aromatic imidazoline derivatives, a number of vasoactive compounds have been studied pharmacologically. Benzylimidazoline (Priscoline®) is the best known vasodilator in this series, and naphthylmethylimidazoline (Privine®) is perhaps the most widely accepted constrictor. Otrivin® 2-(4-tert-butyl-2,6-dimethylbenzyl)-2-imidazoline hydrochloride, is similar to Privine chemically and pharmacologically. Its structural formula is:



"It produces prompt and prolonged mucosal shrinking when applied topically to the nasal mucosa. One drop of a 0.3 percent solution instilled into the rabbit's conjunctival sac produces a marked ischemia lasting for about one hour.

"Toxic effects are those of sympathetic stimulation, including mydriasis, pilomotor excitation, tachycardia, and hypertension, persisting for long periods. One-tenth the acute toxic dose by whatever route was well-tolerated and was repeated daily for 16 days in rabbits. On the other hand, one-fourth the acute lethal dose given daily proved fatal to half the experimental animals within 16 days. In this latter group, morphologic changes were noted in the kidneys; hyperemia and edematous swelling were predominant. Microscopic examination of the spleen, heart, adrenals, intestines, and stomach revealed no pathologic changes.

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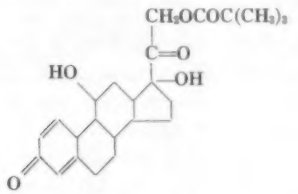
† Ciba Pharmaceutical Products Inc., Summit, New Jersey.

"Ultracortenol® trimethylacetate is 11β, 17α, 21-trihydrox-1,4-pregnadiene-3, 20-dione 21-trimethylacetate with the following structural formula:



"It is odorless, white, crystalline, and insoluble in water."

Experimental studies reported by the manufacturer's Research Department revealed that a single injection of a suspension of Ultracortenol trimethylacetate produced measurable effects, varying in duration from 10 to 20 days.

"One of the major practical uses of the glucocorticoids is based on their anti-inflammatory action. Ultracortenol trimethylacetate, impregnated directly into a pellet before subcutaneous implantation, was very effective in inhibiting granuloma formation, and would exert this action in amounts which did not have general effects on other parts of the body. The results of systemic administration of the steroids on the granuloma formation around sterile pellets were studied. Ultracortenol trimethylacetate inhibited the granuloma formation while producing only slight changes in the adrenal weights or sodium and potassium excretion."

Material

The manufacturer supplied Otrivin in dropper bottles containing 15 cc. of a 0.1-percent solution. A suspension containing 0.5-percent neomycin, 0.05-percent Otrivin, and 0.05-percent Ultracortenol was called Otricorten and was also supplied in 15 cc. dropper bottles.

Preliminary observations were performed on seven persons with normal eyes. Of 88 patients treated with Otrivin and Otricorten, 37 received plain Otrivin and 51 Otricorten. Only 80 patients were followed sufficiently to permit an evaluation of the action of the drug; 34 for Otrivin and 46 for Otricorten. The diagnoses of the patients are enumerated in Tables 1 and 2.

In some of the patients there were two or

TABLE 1

PATIENTS TREATED WITH OTRIVIN

Diagnosis	Dose (times daily)	Duration of Treatment	Therapeutic Results		Irritation after Medication		Effect on Ocular Tension	
			Good	Fair	No	Yes	Unchanged	Not Studied
Conjunctivitis								
a. Acute (1 patient)	4	1 wk.	1		1			1
b. Chronic (10 patients)	1–3	3 to 13 wk.	9	1	10		3	7
c. Allergic (11 patients)	p.r.n. to 3	1 da. to 25 wk.	9	2	11		3	8
Blepharoconjunctivitis (2 patients)	3	1 wk.	2		2		2	
Blepharitis (2 patients)	p.r.n. to 2	3 to 7 wk.	2		1	1	1	1
Lid eczema (2 patients)	2 to 3	1 to 2 wk.	2		2			2
Chalazion (2 patients)	2	2 to 4 wk.	2		2		2	
Hemorrhages (2 patients)	2	14 to 15 wk.*	1	1	2		2	
After cataract operation (2 patients)	p.r.n. to 1	3 to 9 wk.	2		2		2	

* Application continued to study the effect on intraocular pressure.

TABLE 2

PATIENTS TREATED WITH OTRICORTEN

Diagnosis	Dose (times daily)	Duration of Treatment	Therapeutic Results		Irritation after Medication		Effect on Ocular Tension	
			Good	Fair	No	Yes	Unchanged	Not Studied
Conjunctivitis								
a. Acute (3 patients)	2–4	1–2 wk.	3		3		1	2
b. Chronic (6 patients)	1–4	1–10 wk.	4	2	6		1	5
c. Allergic (3 patients)	1–3	2–8 wk.	3		3		2	1
Blepharoconjunctivitis (5 patients)	2–4	1–8 wk.	4	1	3	2	3	2
Hordeolum (4 patients)	1–6	1–2 wk.	4		4			4
Chalazion (3 patients)	1–4	1–4 wk.	2	1	2	1	1	2
Dacryocystitis (2 patients)	2–4 (also injected into lacrimal sac)	2–3 wk.	2		1	1	1	1
Episcleritis (2 patients)	2–4	1–2 wk.	2		1	1		2
Corneal epithelial bulla (1 patient)	3	6 wk.	1		1		1	
Iritis (1 patient)	6 (also atropine)	12 da.	1		1		1	
Secondary glaucoma (1 patient)	3 (also pilocarpine)	6 wk.	1		1		1	
Postoperative cases								
Chalazion (4 patients)	2–4	1–4 wk.	3	1	3	1	2	2
Hematoma (1 patient)	3	2 wk.	1		1			1
Pterygium (2 patients)	2	1–5 wk.	2		1	1	1	1
Muscle operation (also glaucoma) (1 patient)	3 (also pilocarpine)	10 da.	1		1		1	
Enucleation (3 patients)	2	2 wk.	3		3			3
Cataract operation (4 patients) (One also glaucoma)	1–3	4–26 wk.	4		4		4	

more co-existent eye diseases. The tables mention only those ailments which were expected to benefit from the drugs. Some of the patients had glaucoma also and were treated conventionally but were observed for the possible influence of the new drugs on intraocular pressure. In these cases, the usual local and systemic treatment also, if it was necessary, was continued and the eye pressure was checked at different hours of the day, before and after use of Otrivin and Otricorten, respectively. In 35 persons the effect of Otrivin and Otricorten on eye pressure was studied over varying periods up to six months.

METHODS OF STUDY

Both Otrivin and Otricorten were instilled into the conjunctival sac at a frequency corresponding to the severity of the eye affection and for a period corresponding to the indication of the individual case. Thus the treatment lasted from a few days in acute and mild cases to some weeks or even months in chronic or recurrent cases. For blepharitis and lid eczema, the drugs were

either applied superficially to the skin with a cotton applicator or the carefully cleaned finger tip of the patient. Only in one case of dacryocystitis was Otricorten injected into the lacrimal sac.

The manufacturer supplied record sheets which contained space for name, age, sex, diagnosis, dose and duration of treatment; provision was made on the record sheet for recording data regarding the analgesic, anti-infective, anti-allergic and anti-inflammatory properties of the product; and for observations concerning effect on tearing, photophobia, itching and ocular tension. The clinician was asked to note side-effects, and to give his over-all impression of the therapeutic efficacy of the product.

Results

Preliminary observations on seven persons with normal eyes, aged between 23 and 73 years, showed that Otrivin and Otricorten produced no, or negligible, discomfort after instillation of one or two drops into the conjunctival sac. Three persons reported slight smarting or burning of short duration while the others found the fluids to be soothing. Slitlamp examination of the conjunctiva immediately after instillation revealed little or no reactive hyperemia.

A few minutes after instillation, a slight constriction of the conjunctival and episcleral blood vessels was observed on the corneal microscope. This vasoconstriction lasted for about one hour, sometimes longer. A few minutes after instillation the smooth lid muscles produced a widening of the lid fissure amounting to a difference of one to two mm. compared with the width of the intrapalpebral distance of the untreated eye. One 55-year-old man with gray irises showed dilatation of the pupil amounting to one mm. which lasted one hour. In the others, no changes in pupillary size were noticed. The Schiøtz tonometer revealed no change of the intraocular pressure.

With the exception of eight, all patients* seemed to tolerate the drugs very well. One patient complained somewhat about a slight burning of short duration after instillation of Otrivin, and seven after use of Otricorten. In none of these patients was it necessary to discontinue the treatment because of discomfort occurring after instillation. One patient said that Otrivin produced a drawing sensation in the head and ears, while another individual stated that Otricorten made his eye flicker. There were some children in the group, and their answers could not always be considered too reliable. Other patients felt very comfortable under the treatment. One of them stated that the "sandlike" feeling in his eyes cleared after the use of Otrivin.

Therapeutic results were graded according to the objective examination as well as to the subjective response of the patients. The results were excellent or good in all but four of the Otrivin patients and five of the Otricorten patients.

In one case of acute conjunctivitis and one of allergic conjunctivitis, additional treatment became necessary. One subconjunctival hemorrhage reabsorbed as slowly under Otrivin as it would have done without therapy.

In the group treated with Otricorten, two patients with conjunctivitis, one with blepharoconjunctivitis, one with chalazion, and one after lid operation showed only fair results while all others could be classified as good or excellent. One patient who did not co-operate well improved on a combination of Otricorten with Gantrisin. One of the chalazions had to be opened while the others disappeared under the treatment. The patients with subconjunctival hemorrhages were treated only because they insisted on some medication. No evaluation should be made as to efficacy of the agents under such circumstances since no therapeutic results were expected. Some of the patients after cataract extraction experienced marked relief of photophobia with use of Otrivin or Otricorten. A 53-year-old man with conjunctivitis and

* See Tables 1 and 2.

photophobia due to severe nutritional deficiency was not aided by the drops. However, alleviation of photophobia was observed in a 74-year-old poorly nourished woman with a similar diagnosis. I should mention that a very good result was obtained on a 69-year-old ophthalmologist, suffering from episcleritis, who, after two weeks of unsuccessful self-treatment with different drugs, was delighted to notice a definite improvement after administration of Otricorten four times a day for one week.

The anti-allergic action of plain Otrivin, as well as its combination with neomycin and Ultracortenol, was satisfactory throughout. Greater anti-inflammatory action was noticed in the combined suspension than in the plain Otrivin solution. Two glaucoma patients who had reacted to pontocaine instillation with a severe blepharoconjunctivitis responded to Otrivin or Otricorten within a few hours. In many cases, relief of pain or tenderness as experienced by the patient paralleled the regression of signs of inflammation; this was particularly true in postoperative cases. Subjectively, there was relief of tearing, itching and photophobia which again paralleled the improvement which could be noted objectively.

With the exception of rare complaints following drug application, no untoward side-effects were observed.

Intraocular pressure

In 35 persons with normal intraocular pressure or glaucoma normalized by miotics or surgery, intraocular pressure was ascertained before, during, and after medication with Otrivin or Otricorten. The readings were taken with the original Schiøtz tonometer after instillation of 0.5 percent pontocaine solution or butyn in cases which seemed to be allergic to pontocaine, and always with the same instrument.

Fifteen of these patients were treated with Otrivin and 20 with Otricorten. In none of these persons did a pressure increase occur after treatment periods lasting from some weeks to three or more months. The longest observation was for six months on an 82-year-old woman after cataract extraction.

Summary

Although this study, like most reports about therapeutic results, lacks scientifically valid controls, an about equal number of patients with similar eye diseases were treated during this period with combinations of antibiotics, vasoconstrictors, and steroids already on the market. No comparison was available for the unusual corneal epithelial bulla. Also no conjunctival hemorrhages were treated with control drugs.

It can be stated that Otrivin and Otricorten were in no way inferior to, in some cases possibly more efficient than, the already available drugs and that the tolerability and therapeutic effect of Otrivin and Otricorten compared very well with accepted preparations.

5 West Fourth Street (2).

Preparing and writing this article, I was under the impression that it would be the first to discuss ophthalmologic experiences with Otrivin and Otricorten. Five months after submitting my study for publication, I found, in the September issue of The Journal, an article by Dr. Paul Hurwitz entitled "Ophthalmic Otrivin solution" and quoting a paper by the same author published in the EENT Monthly, **32**:140-142 (Mar.) 1953.

NOTES, CASES, INSTRUMENTS

SYMPATHETIC OPHTHALMIA FOLLOWING IRIDENCLEISIS*

CASE REPORT AND INCIDENCE

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INTRODUCTION

The event which prompted this report was an uneventful and successful bilateral cataract extraction in a patient with sympathetic ophthalmia following iridencleisis for open-angle glaucoma.

CASE REPORT

On December 9, 1955, a 72-year-old white woman was referred to the Illinois Eye and Ear Infirmary for the surgical treatment of glaucoma. She had been treated with pilocarpine for three months; otherwise her previous eye history and general medical history were noncontributory.

The relevant eye findings when the patient was first seen were:

Right eye. Corrected visual acuity, 20/20; tension, 25 mm. Hg (Schiøtz) while the patient was being treated with two-percent pilocarpine four times daily. The disc was considered normal in spite of true baring of the blindspot elicited with a 2/1000 white target. The angle was open, the water provocative test was positive (22 to 32) while the patient was receiving pilocarpine (four percent, four times daily), and the coefficient of outflow was 0.10 ml./min./mm. Hg.

Left eye. Visual acuity, 20/30; tension, 34 mm. Hg (Schiøtz) when the patient was receiving two-percent pilocarpine four times daily. The disc was considered normal but the visual field showed a large Bjerrum scotoma to 3/1000 white. The angle was open, the water provocative test was positive (32 to 42) while the patient was receiving four-percent pilocarpine four times daily, and the coefficient of outflow was 0.04 ml./min./mm. Hg. A little nuclear sclerosis was present in each lens.

On December 17, 1955, an iridencleisis after Weekers was performed on the left eye. During surgery there was no evidence of buttonholing the conjunctival flap. The anterior chamber filled with blood from the nasal pillar and no attempt was made to irrigate. Postoperatively the blood was absorbing until the fourth postoperative day when there was a fresh hemorrhage which filled about two thirds of the anterior chamber. On the 12th postoperative day the hyphema had almost completely absorbed and the patient was discharged to her home. At no time during the postoperative course was exposure of the iris noted.

On March 5, 1956 (11 weeks after surgery), the patient was readmitted with a letter from a private ophthalmologist stating that a bilateral iritis had been present for one week. At that time the right eye had a corrected visual acuity of 20/40 and the tension was 20 mm. Hg (Schiøtz). Scattered large keratic precipitates and posterior synechias were present. No fundus lesion was seen. The left eye had a corrected visual acuity of 20/100 with a tension of 20 mm. Hg (Schiøtz). Numerous large and small keratic precipitates were present mainly on the lower part of the corneal endothelium. Koeppe nodules were present at the pupillary border, in addition to some posterior synechias. No fundus lesion could be seen through the hazy vitreous. An intradermal test with uveal pigment was performed and the skin area of the test was biopsied and described as follows:

Gross. The specimen consists of an ellipse of tissue with a gray-white periphery and a light blue central portion. It is submitted formalin-fixed and measures 1.2 by 0.5 by 0.3 cm. embedded.

Microscopy. The section shows normal epithelium, hair follicles and sweat glands. In the dermis are scattered phagocytes with dark-brown pigment contained and a marked lymphocytic reaction. There are a number of large multinucleated giant cells. Lymphocytes are also seen around nearby blood vessels.

Diagnosis. Marked lymphocytic reaction to uveal pigment in the dermis.

The patient was treated in the hospital for one month with topical atropine and Hydrocortone in both eyes. The condition improved slightly and the vision in the left eye was 20/40 when the patient was discharged from the hospital.

On April 24, 1956, the patient was readmitted to the hospital. Following is the resident's (Robert Lamberson, M.D.) very descriptive admission note:

"The patient was led back into the hospital this afternoon, 25 days after having been discharged in a quiescent state with 20/40 vision in each eye and 128 days after operation for glaucoma. All useful vision has been lost. There is now a heavy beam in each anterior chamber, and there is bilateral posterior segment involvement to such an extent that no fundus details are visible despite the fact that there is, as yet, little increase in her lens changes."

Both eyes were soft and there was a heavy beam in each anterior chamber. The vitreous showed diffuse opacities and much swirling debris in each eye. The fundus could not be seen in either eye by direct ophthalmoscopy. By indirect ophthalmoscopy,[1] the left fundus was seen and no pathologic change noted. The patient was treated in

* From the Department of Ophthalmology, Illinois Eye and Ear Infirmary, University of Illinois, Chicago, Illinois.

the hospital for one month with Meticorten (30 mg. daily), local mydriatics and local steroids. The visual acuity was 20/100 in each eye on discharge and there was some clearing of the vitreous haze. She was discharged on Meticorten and local mydriatics and steroids.

During the next year the patient was followed by a private ophthalmologist who continued to treat the patient with small doses of Meticorten and local mydriatics and steroids, which kept the uveitis under control and the tension remained within normal limits in both eyes.

In July, 1957, the patient was readmitted to the hospital with an acute exacerbation of her uveitis following total withdrawal of steroids. After the administration of Meticorten (15 mg. daily for one week), the visual acuity in the right eye rose to 20/100 and remained at 20/200 in the left eye.

In September, 1957, the tension in the right eye was 36 mm. Hg (Schiøtz) and the patient was put on miotics. By June, 1958, the tension had risen to 60 mm. Hg (Schiøtz) and the administration of Diamox was begun which brought the tension into the middle thirties. Gonioscopy of the right eye failed to show any of the angle structures, and the angle was described as closed through 360 degrees due to iris bombé. The lens had a posterior subcapsular cataract and moderate nuclear sclerosis.

On July 12, 1958, when the tension of the right eye was 24 mm. Hg and the visual acuity 8/200, right intracapsular lens extraction with a full iridectomy was performed. The postoperative course was uneventful and the patient was discharged on the 12th postoperative day when the visual acuity of the right eye was 20/100. Since the right lens extraction, the tension in that eye has been well controlled.

On April 6, 1959, when the left visual acuity was 20/200, left intracapsular lens extraction was performed without vitreous loss. The iridencleisis was left undisturbed by placing the incision in the cornea from the 11- to 1-o'clock position and at the limbus from the 9- to 11-o'clock and 1- to 3-o'clock positions. In spite of the fact that the patient was taking Meticorten there was more than usual increase in the beam and cells in the left eye postoperatively but the course was otherwise uncomplicated.

When the patient was last seen on November 3, 1959, the eye findings were:

Right eye. Visual acuity, 20/50; tension, 24 mm. Hg (Schiøtz). The anterior chamber showed a mild beam and no cells. There was a full iridectomy and the eye was aphakic. The fundus was seen with 20/20 clarity and the disc showed almost total glaucomatous cupping, the macula was normal and the AV ratio was 1:3. In the peripheral fundus were many round, circumscribed areas of choroidal atrophy, each being about half a disc diameter.

Left eye (seven months postoperative). Visual acuity, 20/70; tension, 19 mm. Hg (Schiøtz) with the filtering bleb at the 12-o'clock position still present. The anterior chamber had a mild beam and no cells. The fundus was seen with 20/20 clarity; the disc showed pathologic cupping and there were circumscribed areas of choroidal atrophy in the periphery.

Summary. The eye history of a 75-year-old woman is presented. Over three years previously she had had an iridencleisis after Weekers for open-angle glaucoma; within 10 weeks she developed a bilateral granulomatous uveitis with marked clouding of the vitreous. Biopsy of an intradermal test with uveal pigment showed that the pigment had been engulfed by phagocytes. The uveitis was controlled with corticosteroids. The patient has had a bilateral lens extraction with a resultant visual acuity of 20/50 in the right eye and seven months postoperatively 20/70 in the left eye.

Incidence of sympathetic ophthalmia

1. Previously reported

Friedenwald, et al.,[2] quote the incidence of sympathetic ophthalmia following cataract extraction and trephining operations as one to two per 1,000, and five to 10 per 1,000 following iris-inclusion operations. Mackie and Rubenstein[3] reviewed 2,000 published cases of iridencleisis with an over-all incidence of 0.2 percent of sympathetic ophthalmia. In their own series of 110 cases of iridencleisis, two women patients developed sympathetic ophthalmia, an incidence of 1.9 percent.

2. At the Illinois Eye and Ear Infirmary

Between January 1, 1949, and June 30, 1958, a total of 319 iridencleisis operations were performed. Twenty-seven patients who were followed for less than three months were excluded because the case herein reported developed sympathetic ophthalmia about 10 weeks after surgery and Mackie and Rubenstein's[3] cases were diagnosed nine weeks after surgery. Three surgical procedures were omitted because of unsatisfactory records. Attempts to contact these patients were unsuccessful but in each case attending men and/or the resident was contacted, and none was able to recall the development of sympathetic ophthalmia. There remained a total of 289 iridencleisis operations on patients who were followed for three months to nine years; of these pa-

tients, only one (the case reported above) developed sympathetic ophthalmia.

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ACKNOWLEDGMENT

I wish to express my gratitude to Peter C. Kronfeld, M.D., for encouraging me to write this paper.

REFERENCES

1. Brockhurst, R. J.: Modern indirect ophthalmoscopy. Am. J. Ophth., **41**:265, 1956.
2. Friedenwald, J. S., et al.: Ophthalmic Pathology. Philadelphia, Saunders, 1952, p. 127.
3. Mackie, E. G., and Rubenstein, K.: Iridencleisis in congestive glaucoma. Brit. J. Ophth., **38**:641, 1954.

VASCULITIS RETINAE IN LEPROSY*

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Vasculitis retinae (Eales' disease) with recurrent intraocular hemorrhages accompanied by perivascular exudates in young adults is probably not a disease entity per se, but rather a clinical sign common to many diseases.[1,2] Other names for this condition are periphlebitis retinae[3] and angiopathia retinae juvenilis.[4]

Many etiologic factors are mentioned in the literature including tuberculosis, sarcoidosis, thrombangiitis obliterans (Buerger), focal infections, lues, endocrine factors, diseases of the hemopoietic system and miscellaneous other groups. Leprosy is not mentioned as an etiologic factor. A case of periphlebitis retinalis with recurrent vitreous hemorrhages in a leprotic patient is now described.

CASE REPORT

A. I., a 25-year-old man, was born in Turkey. At the age of 12 years, while he was in Turkey, the first symptoms of leprosy appeared, consisting of small nodules on the face and prolonged bleeding from the nose. He was treated in a hospital where he was given chaulmoogra. Two years later on his immigration to Israel he was immediately admitted to the Hansen Hospital in Jerusalem. The patient showed leprous nodules on the nose, ears, breast and hips. Both eyes showed marked leprotic lesions: superficial punctate keratitis, pannus, anesthesia of the cornea, atrophic iris and posterior synechias. The right eye had seclusion of the pupil and it was not possible to see the fundus. The fundus of the left eye showed no abnormalities. The vision in both eyes was 5/15 to 5/12. Later the patient was treated as an ambulatory case and the ocular lesions remained stationary.

Masses of lepra bacilli were found till 1944 in the mucous membrane of the nose, smears from the earlobes and from the various lesions of the body. From 1944 the bacteriologic examination has been negative. Leprosy bacilli were not found in conjunctival smears. The histologic examination of the lesions showed lepromatous granuloma.

In April, 1959, the patient suddenly felt blurring of the vision in the left eye, which was reduced to counting fingers at a distance of one meter. Bleeding into the vitreous and into the retina near the papilla and exudates around the engorged inferior temporal vein were found. After four weeks the vitreous hemorrhage cleared up and the blood near the papilla resorbed markedly. In June, 1959, a recurrence of the hemorrhage also cleared up within a short time. In September the hemorrhage in the vitreous was nearly totally absorbed (fig. 1). Only a small hemorrhage in the retina could be seen but the exudates around the inferior temporal vein still existed. The vision improved to 5/20 to 5/15. The treatment consisted of PAS, streptomycin and thiosemicarbazone.

General medical and neurologic examinations showed no pathologic findings other than leprosy. No clinical and X-ray signs of tuberculosis of the

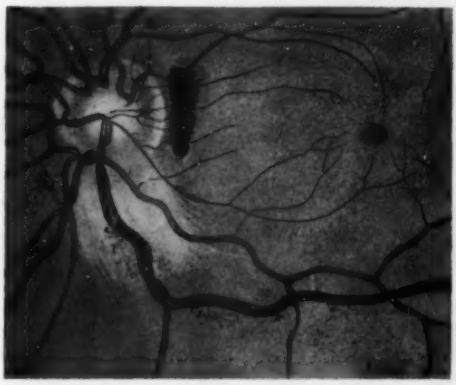

Fig. 1 (Landau). Vasculitis retinae (Eales' disease) in a leprous patient. Fundus of the left eye.

* From the Department of Ophthalmology, Hadassah-University Hospital, and the affiliated Hospital for Hansen's Disease, Ministry of Health.

lungs were found. Wassermann and Kahn tests in blood and cerebrospinal fluid were negative. Blood findings were: hemoglobin 12.5 gm., erythrocytes 5,000,000. Sickle cells were not found. Blood chemistry was normal. Mantoux test in 1950, 1/50,000 negative; in 1952, 1/10,000 weakly positive; in 1959, 1/10,000, strongly positive, 1/50,000 positive, 1/100,000 doubtful. Kveim test was negative. No septic focus was found on dental and otolaryngologic examination.

Discussion

Many theories about the etiology of Eales' disease have developed. Eales[5] referred to it as primary vitreous hemorrhage of unknown etiology. The etiologic significance of tuberculosis was first stressed by Axenfeld and Stock,[6] but serious objections to this view were made by Marchesani[7] who associated the condition with thrombangiitis obliterans. Ballantyne and Michaelson[8] reported a case in which no specific etiology could be found. Congenital or acquired lues was recognized as one of the most important factors in the older literature.[2] Sarcoidosis[9] as a possible cause has been mentioned but most of the reported cases were not of the usual type with recurrent hemorrhages but were periphlebitis secondary to an anterior uveitis. Various endocrine factors have been associated with recurrent hemorrhages in the vitreous but an endocrine etiology has little support. Disorders of the hemopoietic system in connection with recurrent hemorrhages of the retina and in the vitreous have also been reported,[2] as have such miscellaneous etiologies as malaria, parasites, vitamin-C deficiency, toxoplasmosis, and Behçet's disease.

The patient presented in this report showed no evidence of any of these conditions except a strongly positive Mantoux test. Since no other signs of tuberculosis were found, there is no definite evidence of tuberculosis as an etiologic factor. It is known that patients with para-allergic reactions to lepromin may have positive Mantoux tests. In the modern fight against leprosy BCG inoculations are performed to immunize against lepropsy. BCG may convert the nonreactor into a positive reactor with a positive lepromin test.[10]

It seems therefore not unlikely that the phlebitis retinae in this case was associated with the leprosy. The retinal changes may be the result of the presence of the bacillus in the retina or may be an allergic manifestation to the presence of the organism elsewhere in the body. Loewenstein, Michaelson and Hull[11] discussed the possible role of allergy in vasculitis retinae in the young.

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Acknowledgment

I wish to thank Prof. F. Sagher and Dr. J. Szeskin for their helpful co-operation, and Mr. M. Ivry for the drawing of the fundus.

References

1. Duke-Elder, W. S.: Textbook of Ophthalmology: v. III. London, Henry Kimpton, 1954, p. 2602.
2. Donders, P. C.: Eales' disease. Documenta Ophth., **9**:1-105, 1958.
3. Perls, M.: Zur Kenntnis der Tuberculose des Auges. Arch. f. Ophth., **19**:221-249, 1873.
4. Cords, R.: Zur Kenntnis juveniler Netzhautgefaesserkrankungen. Ztschr. Augenh., **26**:441-449, 508-520, 1911.
5. Eales, H.: Cases of retinal haemorrhages associated with epistaxis and constipation. Birmingham M. Rev., **9**:262-273, 1880; Primary retinal haemorrhage in young men. Ophth. Rev., **1**:41-46, 1882.
6. Axenfeld, Th., and Stock, W.: Ueber die Bedeutung der Tuberculose in der Aetiologie der intraocularen Haemorrhagien und der proliferierenden Veraenderungen der Netzhaut, besonders ueber Periphlebitis retinalis bei Tuberculoesen. Klin. Monatsbl. f. Augenh., **49**:28-35, 1911.
7. Marchesani, O.: Juvenile rezidivierende Glaskoerperblutungen und Thrombangiitis obliterans (Buerger). Ber. Ophth. Ges. Heidelberg, **50**:54-63, 1934.
8. Ballantyne, A. J., and Michaelson, I. C.: A case of perivasculitis retinae associated with symptoms of cerebral disease. Brit. J. Ophth., **21**:22-35, 1937; Some aspects of disease affecting the retinal veins. Tr. Ophth. Soc. U. Kingdom., **67**:59-91, 1947.
9. Weve, H. J. M.: Oogaandoeningen bij de ziekte van Besnier-Boeck-Schaumann. Verslagen der Tuberculose-Studie-Commissie van de Nederl. Centr. Vereniging tot Bestrijding der Tuberculose, No. 22, 1948, p. 1-36.

10. Sagher, F.: Leprosy: Review of literature from late 1954 to early 1956. Dermatologica, **115**:780-808, 1957.
11. Loewenstein, A., Michaelson, I. C., and Hull, J.: Retinal vasculitis of the young: A pathological report. Tr. Ophth. Soc. U. Kingdom, **46**:211-230, 1946.

CHOROIDOSCOPY*

A SUPPLEMENTARY TECHNIQUE TO OPHTHALMOSCOPY

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The following technique of examination of the fundus by means of combined transillumination, scleral depression and the indirect ophthalmoscope (Schepens or Keeler type of binocular ophthalmoscope) has been employed and found quite useful as well as simple.

Indirect ophthalmoscopy is performed as conventionally described for the Keeler or Schepens scope. That is, a convex lens is held in one hand about two inches in front of the patient's eye with the examiner one and one-half to two feet from the patient (figs. 1 and 2). The bright overhead binocular ophthalmoscope light is not used. An ordinary May head light from a monocular ophthalmoscope (fig. 3) or a standard transilluminator is placed with the other hand over the eyelids (as deep under the orbital rim as possible) or over the anesthetized globe deep in the fornices of the different quadrants. Scleral depression can be done simultaneously with use of this transilluminator or May head bulb and all peripheral parts of the fundus (including ora serrata, pars plana and even ciliary processes), as well as the posterior fundus, are well visualized.

This technique has been used in cases in which cloudy media or moderately dense cataracts prevented visualization of the fundus by routine indirect binocular ophthalmoscopy, including scleral depression. However, by means of combined transillimination

Fig. 1 (Cohen). Using the May ophthalmoscope light as a transilluminator, together with the unilluminated binocular ophthalmoscope and hand lens, as in indirect ophthalmoscopy.

and scleral depression, the structures become quite easily visible through the cloudy media. Furthermore, the choroidal vascular structure and pigmentation come into clear view and whorls of choroidal veins have been seen (or so interpreted) emptying into their vortex veins, as well as the straight, horizontally coursing, long ciliary vessels running anteriorly. Peripheral retinal tears or holes or dialyses are also easily picked up by the

Fig. 2 (Cohen). Another view showing described technique.

* From Ophthalmology Division of the Jewish Hospital of Brooklyn.

Fig. 3 (Cohen). The May head removed from its light source.

sharp contrast in light intensity under the tear. Peripheral hemorrhages, tumors and detachments can also be visualized.

Patients are not so irritated by this method as by an intense dazzling overhead binocular ophthalmoscope light. Moreover, the fundus view is not hampered by reflections of the light source from the surfaces of the condensing lens and the cornea. A widely dilated pupil, even though preferable, is not required. I have even done successful examinations in the presence of very contracted (glaucoma-treated) pupils. It has been noted that the pupil frequently dilates somewhat under scleral transillumination. Patients are usually not bothered by the technique. At most, they may complain after a while of a little warmth over the eye. In such cases the light is turned off and the bulb allowed to cool, or a "cold" light bulb may be used.

The retinal vessels are not visualized as clearly as with the conventional indirect ophthalmoscope. Nevertheless, this technique is a useful supplement to the routine method and offers good peripheral visualization through cloudy media as well as affording a means to study the choroidal layer and vasculature. This technique has also been applied to gonioscopy, for which the transilluminating light is placed just adjacent to the limbus and the gonioprism rests on the anesthetized cornea. By this means, good contrast visualization of the anterior chamber angle and Schlemm's canal is obtained even in the presence of a cloudy cornea.

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CHLORAL HYDRATE*

A USEFUL PEDIATRIC SEDATIVE

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With dismaying frequency, the eye clinic and the practicing ophthalmologist face the challenge of contending with an infant or a very young child. The prospects of performing satisfactory ophthalmoscopy, measuring the ocular tension, removing sutures and, in young children, probing the lacrimonasal duct, are usually bleak. Based on previous experiences, these procedures suddenly loom harrowing and the latter two may be fraught with some danger.

Attempts at solving the problem usually fall in two categories: general anesthesia or heavy sedation. General anesthesia will get the job done; however, because of its expense, the loss of time entailed, and its inherent dangers, it is not always practical.

Various sedatives have been used with questionable success. The one presently in vogue is pentobarbital (Nembutal). It is a rapid-acting barbiturate of medium range. Because of its extremely bitter taste it cannot be satisfactorily masked for pediatric oral use. Consequently, it is generally used as a suppository. Since its rate of absorption depends on the stool content of the rectum, the sedative effects are unpredictable. Frequently there is either no sedation or too much. Furthermore, it is not uncommon to produce an undesirable long-lasting stage best described as "drunkedness." This precludes the performance of the procedure; in addition, because the infant acts "strange and wild" for several hours, the situation creates marked parental distress.

In search for a better oral hypnotic, chloral hydrate syrup† was given in a clinical trial.

* From Division of Ophthalmology, Department of Surgery, University of Arkansas Medical School, Little Rock, Arkansas.

† A preparation made by our pharmacy which is similar to Squibb's Noctec.

It is fairly pleasant tasting and most patients accept it with only a minimum of struggle. Moreover, it usually stays down. It is prepared in a thick, clear liquid containing approximately 100 mg./cc. For average-sized infants the dose is 25 mg. per month of age. The lethal dose for children is 5.0 to 10 gm.[1]

A five-cc. syringe is used to measure and administer the sedative. This is accomplished by inserting the glass tip of the syringe in the corner of the mouth and slowly allowing the medication to gravitate in. To keep the patient from spitting it out, the free hand is used to squeeze the cheeks together in order to prevent closure of the mouth. A few sips of milk or any other suitable liquid help to wash the syrup down, further mask the taste and pacify the infant. Deep sleep ensues within 30 to 45 minutes. Most of the patients are fully awake two hours later. Hang-over and side-effects are rare.

I have used this hypnotic agent for the past 18 months and have found it safe, inexpensive, well tolerated and very effective. In conjunction with the appropriate topical anesthetic, sedation with chloral hydrate has permitted the execution of the procedures already mentioned in nine out of every 10 infants. It merits a place in the armamentarium of those who face the task of dealing with infants and young children.

109-110 Queens Boulevard (75).

Reference

[1] Drill, V. A.: Pharmacology in Medicine. New York, 1958, ed. 2.

PLASTIC REPAIR OF EYELID MARGIN*

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Congenital coloboma, marginal injuries and wounds producing various types of defects of the superior lid margin are frequent but vary considerably depending on their cause. Various plastic operations for their repair have been published.

The technique of Wheeler[1] is often used in cases of eyelid coloboma. Fox's[2] techniques are used in marginal notches and in marginal lunate defects of the eyelids.

In the case herein presented, which showed a large lunate defect of the right superior eyelid, these techniques did not seem suitable because the defect was so wide. Therefore, the operation to be described was planned for use in this case (figs. 1 and 2, before the operation; fig. 3, after operation).

Case report

Mr. A. D., aged 27 years, an officer, had a large lunate defect of the right superior eyelid margin resulting from an oriental sore 20 years earlier. He came to our clinic on April 1, 1959, for the treatment of lagophthalmic keratitis in the right eye, due to the eyelid defect. After treatment of the keratitis, vision increased to 2/10 from 1/10. However, it was decided to repair the eyelid defect to prevent a relapse of the lagophthalmic keratitis.

Operative technique

1. An incision is made at the intermarginal groove of the eyelid which contains the defect, near the lacrimal punctum to the external canthus (fig. 4).
2. The skin and orbicularis muscle are dissected from the tarsus (fig. 5).

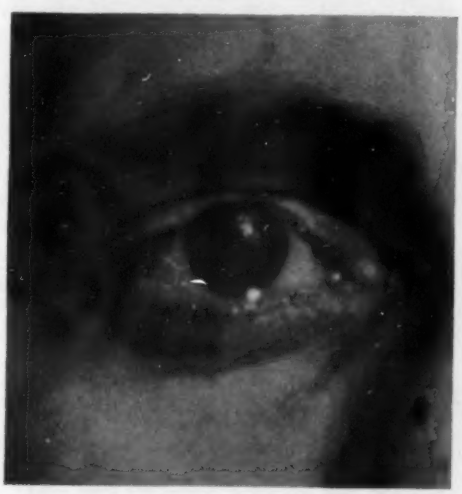

Fig. 1 (Erbakan). Patient before operation.

*From the Eye Clinic of the Medical Faculty, University of Ege.

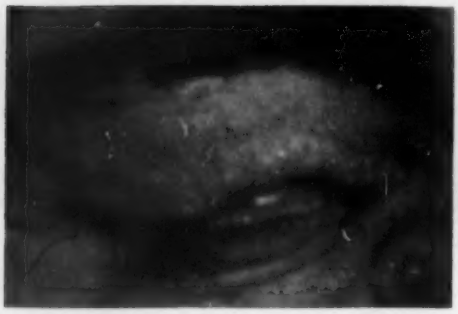

Fig. 2 (Erbakan). Patient before operation.

Fig. 3 (Erbakan). Patient after operation.

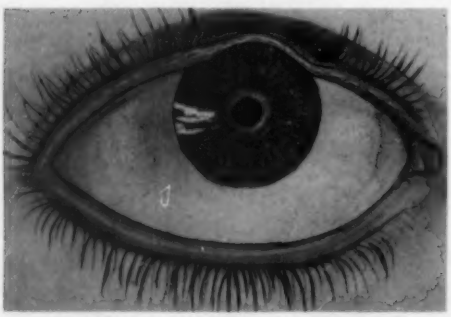

Fig. 4 (Erbakan). Incision in intermarginal groove of eyelid.

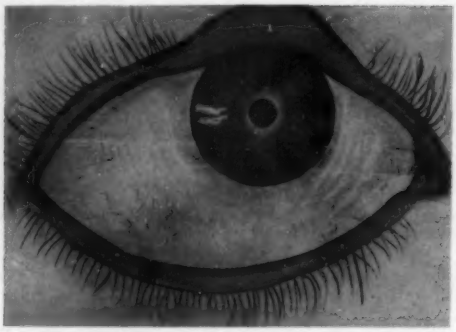

Fig. 5 (Erbakan). Skin and muscle dissected from tarsus.

Fig. 6 (Erbakan). A T-shaped incision is made on the tarsus.

Fig. 7 (Erbakan). The horizontal arm of the T-shaped incision is longer than the vertical.

Fig. 8 (Erbakan). The dissected parts of the tarsus are sutured into each other.

3. An incision is made on the tarsus in the form of "T" the horizontal arm of which is longer than the vertical (figs. 6 and 7).

4. The two dissected parts of the tarsus are sutured into each other to achieve the normal width (fig. 8).

5. The skin incision is lengthened from the external canthus and a small-triangular piece of skin is removed (fig. 9).

6. The defect and incisions in the temporal region are sutured. Two double-armed sutures are used to close the skin and tarsus (fig. 10).

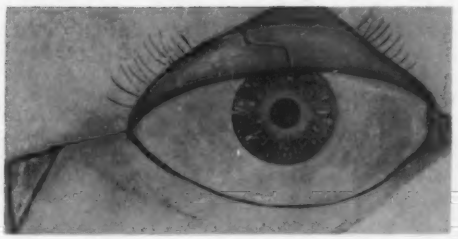

Fig. 9 (Erbakan). A triangular piece of skin is removed.

Fig. 10 (Erbakan). Two double-armed sutures are used to close the wound.

This type of plastic operation was not described in any of the classical surgery books and journals available to me. Since the results in the case here reported were most satisfactory, a description of the technique seemed justified.

Ege University Eye Clinic.

REFERENCES

1. Arruga, H.: Ocular Surgery. New York-Toronto, London, McGraw-Hill, 1956, p. 169.
2. Spaeth, E. B.: Principles and Practice of Ophthalmic Surgery. Philadelphia, Lea, 1948, ed. 4, p. 365.

ADAPTATION OF SLITLAMP TO INDIRECT OPHTHALMOSCOPY*

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During slitlamp microphthalmoscopy, the observer may fail to locate a lesion that has been previously seen ophthalmoscopically. If one then attempts to obtain a wide field by widening the slitbeam, the fundus view becomes fogged and details are lost. This fogging is due to the light beam illuminating a wide area of the cornea, leaving almost no area for observation (figs. 1 and 2). Since light is scattered in the corneal tissue, any overlapping of the incident and reflected beams will fog the fundus picture. Thus, if orientation is lost during slitlamp examination of the fundus, the patient has to be moved away from the slitlamp apparatus to be re-examined by the usual methods of ophthalmoscopy.

The aim of this paper is to describe a method for indirect ophthalmoscopy through the corneal microscope, using the slitlamp as a source of diffuse illumination of the fundus so that one can shift from binocular indirect ophthalmoscopy to slitlamp microphthalmoscopy without interruption. This has been achieved by adding, in the path of the slitbeam, a diverging lens that will cause the convergent slitlamp rays to come out as a parallel beam. This latter beam will then meet my supplementary lens (+55 or +60D.) used for slitlamp examination of the fundus (El Bayadi[1,2]) and will come to a focus in the center of the cornea of the examined eye. By such an arrangement the image of the slit, markedly reduced in size, will be sharply focused on only a small area of the cornea, leaving the entire lateral halves unilluminated and free for ophthalmoscopy through both arms of the microscope (fig. 3).

APPARATUS AND METHOD

As for slitlamp examination of the fundus, the apparatus used should permit marked reduction of the illumination-observation an-

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Fig. 1

Fig. 2

Fig. 3

Figs. 1 to 3 (El Bayadi). (1) Area of the cornea occupied by the narrow slitlamp beam: (a) lateral illumination; (b) central illumination. (2) Area of the cornea occupied by the wide slitbeam: (a) lateral illumination; (b) central illumination. There is almost no clear space for observation. (3) Area of the cornea occupied by beam when the new concave lens is placed in front of the slitlamp prism: (a) lateral illumination; (b) central illumination. Ample space is available for observation.

gle. It is preferable to use an apparatus of modern construction where the slitlamp can be moved across the microscope without interruption.*

With the pupil sufficiently dilated, the patient should be comfortably seated before the slitlamp, holding the hand bars firmly to support his hands and help head fixation. The chin-head rest should be moved back so that the distance between the microscope and examined eye be increased by almost 3.0 cm. more than for conventional microscopy of the anterior segment. In the path of the slitbeam, a concave lens is interposed which will allow the rays to form a parallel beam. For the Ziess slitlamp such a lens should be about −15D. (when placed just in front of the slitlamp prism). Provision may be made to incorporate such a lens within the optics of the slitlamp, in the same way as a red-free filter, or it may be fixed in front of the slit-

* In fairness, I must point out that this important improvement was first available in the apparatus of the Allied Instrument Manufacturers of London.[3] It was adopted by Zeiss on the Littmann[4] slitlamp in 1950. It appeared on the Haag-Streit slitlamp on the "900" model which came out late in 1959.

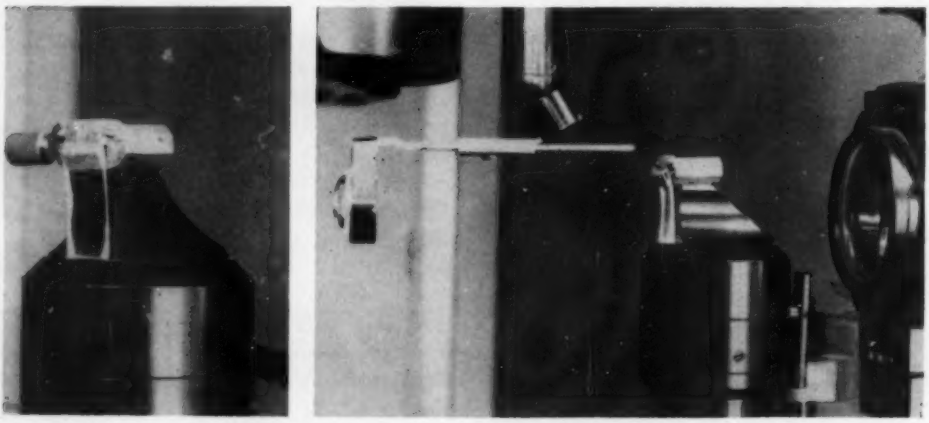

Fig. 4 (El Bayadi). The concave lens attached to the slitlamp prism.

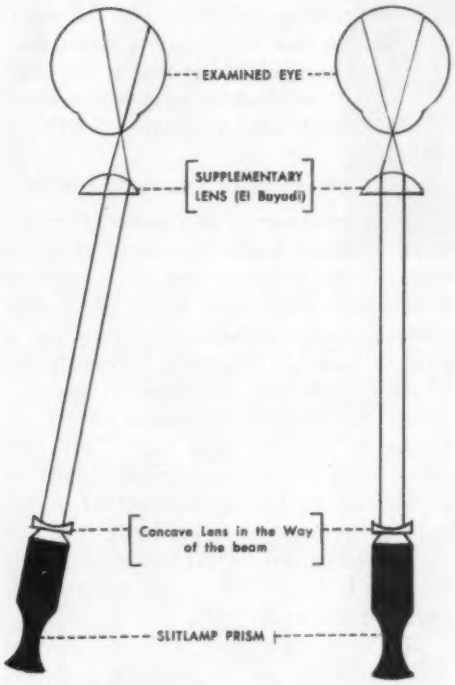

Fig. 5 (El Bayadi). The path of the illuminating beam for indirect ophthalmoscopy in diffuse light using the slitlamp apparatus.

lamp prism in a similar way to the rotating prism of the Zeiss apparatus and provision made to swing it out of the way when not required (fig. 4).

The light beam—now parallel—is directed to the convex supplementary lens and is made to focus in the center of the cornea (fig. 5). To achieve this the supplementary lens should be about 16 mm. away from the cornea, that is, a distance equal to its own focal length. If now the slit is widened, the illumination of the fundus is increased, but this will not interfere with observation in any way since the illuminated part of the cornea is always very small. With my convex supplementary lens the illumination of the fundus is often too intense and can be reduced by narrowing the slit or by lowering the intensity of the lamp through the rheostat.

Stereoscopic examination is then carried out by the microscope and, by various movements of the examined eye and the supplementary lens, the entire fundus can be quickly examined out to the periphery. As suggested by Rosen[5] scleral indentation may be combined to examine the region of the ora serrata. Higher magnification may be used as required.

The fundus lesion is now brought into the center of the field and the new lens, which is in the way of the beam, is swung out of its way. Without any further adjustment the fundus lesion is now seen in optical section. A central position of the lamp is preferable for ophthalmoscopy but for slit examination of the fundus a lateral illumination improves the resolving power of the image as regards depth perception.

Ramses Building, Midan Ramses.

References

1. Bayadi, G. El: Brit. J. Ophth., **37**:625, 1953.
2. ———: Acta XVII Internat. Cong. Ophth., **1**:100, 1954.
3. Binstead: Allied Instrument Manufacturers, London, personal communication, 1953.
4. Littmann, H.: Am. J. Ophth., **33**:1863, 1950.
5. Rosen, E.: Am. J. Ophth., **48**:782, 1959.

STANDARDIZED SCHIRMER TEAR TEST KIT*

G. Peter Halberg, M.D.,
AND
Conrad Berens, M.D.
New York

The use of small strips of filter paper for estimating the amount of tear fluid produced during a given period of time was first proposed by Schirmer in 1903.[10] This test has been used by many ophthalmologists and has become a valued diagnostic procedure in practice. Exhaustive appraisals of the results obtained with the test when used in a variety of conditions have been published by such distinguished authors as Bruce,[4,5] de Roetth,[6–9] and many others.

Classical Schirmer test

The test is usually performed by cutting Whatman No. 41 filter paper into 35 mm. by 0.5 mm. strips. The first four to five mm. at one end of the paper strip serve as a wick and, when bent, as a hook for the eyelid. This portion of the strip is not included when the length of the moistened strip is measured.

For the test, the patient sits upright in the examining chair. After reassuring him that a painless test is to be performed, the physician hooks the bent wick end of the paper strip on the margin of the lower eye lid at the junction of the outer and middle one third. The time is noted and the patient is asked to close his eyes if he finds this more comfortable. Some patients prefer to continue to blink at the usual rate. Only in extremely sensitive patients is it necessary to touch the area of insertion lightly with a cotton swab soaked in a tropical ophthalmic anesthetic. Active squeezing of the eye lids is discouraged. Great care should be exerted to avoid touching the cornea with the paper strip because this could cause a reflex flow of tears. The usual testing time is five minutes but, if the flow of tears is excessive, three minutes or even a minute may suffice.

Standardization of the paper strips

An informal survey of a number of practicing ophthalmologists disclosed that all of them use the Schirmer test, some applying it more often than others. When asked, most ophthalmologists admitted that they use a piece of clean but nonsterile Whatman No. 41 filter paper and cut strips to approximately the classical dimensions. Others informed us that any filter paper "will do." These informal communications served as an impetus to the development of standardized sterile strips in kit form. It is our understanding that no tear-testing kit of this type was or is available in this country or in any other part of the world.

The basic departures from the classical Schirmer strips are the following features: (1) Standardized, highly absorbant filter paper; (2) rounded end at the conjunctival portion of the strip; (3) notch at the transition area between the wick surface and the testing surface of the strip; (4) sterility.

We found the No. 589 black ribbon filter paper to be very similar to Whatman No. 41 filter paper. These are described by their manufacturers* as having an alpha content of 96 percent, which is the purest and highest grade of cotton fiber and consisting of the highest grade alpha cellulose available because the paper has no additives.

Our findings with No. 589 black ribbon paper showed that it is a highly absorbent filter paper. It absorbs about 10 lambdas† of tear fluid per 20 mm. of the strip, which corresponds to 0.5 lambda per mm.

We found the rounded conjunctival end convenient and a definite advantage over the

* Aided by a grant from the Iso-Sol Company and The Ophthalmological Foundation, Inc. The technical co-operation of the Iso-Sol Company, Lindenhurst, New York is gratefully acknowledged.

* Carl Schleicher & Schuell Company, Keene, New Hampshire.

† 1.0 lambda = 0.001 ml.

Fig. 1 (Halberg and Berens). The tear test kit. (Instruction sheet not shown.)

angulated corners which might be traumatic or irritating.

The notch at the point of transition from the wick area into the testing area of the strips is a convenient feature for identifying the line for folding the filter paper. Later when measuring the moistened strip, the notch serves as a starting point for the measurement.

Excision of a diagonal piece from the distal end of the testing area of one of the paired strips permits easy differentiation of which paper was inserted in the left or the right eye. We recommend using the angulated strip always for the right eye.

Sterility is assured because the clean strips are exposed to a mixture of 10-percent ethylene oxide and 90-percent carbon dioxide gas under 15 lb. pressure per square inch for eight hours before being heat-sealed in the sterile transparent polyethylene envelopes. These plastic containers also help to prevent contamination of the wick, since the folding of the rounded wick at its junction with the testing segment may be performed within the sealed transparent envelopes.

The plastic envelopes may also serve as convenient shipping containers when tear samples must be forwarded for electrophoretic studies in the laboratory. When using the envelopes for shipping purposes, only one of the short sides is cut open with scissors. After the moistened strips containing the tear sample are placed in the plastic container, the cut side can be folded and sealed with cellophane tape.

The strips are paired in individual transparent plastic envelopes. Five pairs are supplied in a paper envelope on which is printed a millimeter scale for convenience in measuring the moistened strip. A detailed instruction sheet is enclosed within the paper envelope. These kits were used during the past several months by a number of ophthalmologists on an experimental basis. The majority of those who reported were favorably inclined.

Indications for the test

A carefully performed Schirmer test will often reveal a lowered secretion of tears which could be the cause of several ocular complaints, for example, dryness, a feeling of a foreign body, burning, and sandy or gritty sensation in the eyes. It is our belief that this test should be performed before corneal transplantation, cataract surgery and prior to fitting contact lenses. It should be kept in mind that even patients who complain of "tearing" may have a lacrimal dysfunction.

Evaluation of findings

If the moistened portion of the strip cannot be easily visualized, it should be held in front of a light.

A measurement of 15 mm. (length of moistened area from the notch) in each eye is regarded as standard for normal tear production. Above the age of 40 years, normal values will vary between 10 and 15 mm. Measurements below 10 mm. in either eye should be given careful consideration, and in the majority of these patients, true dysfunction of tear production will be revealed.

Summary

A standardized Schirmer tear test kit is described. It consists of sterile, standardized filter paper strips that are precut to proper size, have rounded ends for conjunctival contact, are notched for easier measurement, and are sealed in a transparent plastic bag. They are supplied in five sets of two strips each in a paper envelope on which is printed a mm. scale and accompanied by a detailed instruction sheet.

936 Fifth Avenue (21).
708 Park Avenue (21).

References

1. Adler, F. H.: Physiology of the Eye. St. Louis, Mosby, 1950.
2. Balik, J.: The lacrimal fluid in keratoconjunctivities sicca: A quantitative and qualitative investigation. Am. J. Ophth., **35**:773, 1952.
3. Beach, S. J.: In The Eye and Its Diseases (Conrad Berens). Philadelphia, Saunders, 1950, ed. 2, p. 156.
4. Bruce, G. M.: Keratoconjunctivities sicca. Tr. Am. Ophth. Soc., **38**:149, 1940.
5. ———: Keratoconjunctivites sicca. Arch. Ophth., **26**:945, 1941.
6. de Roetth, A., Sr.: On the hypofunction of the lacrimal gland. Am. J. Ophth., **24**:20, 1941.
7. ———: Hypofunction of lacrymal gland and Sjoegren's syndrome. Lancet, **65**:423, 1945.
8. ———: The dry eye. Acta XVI Conc. Ophth., London, **1**:456, 1950.
9. ———: Lacrimation in normal eyes. AMA Arch. Ophth., **49**:185, 1953.
10. Duke-Elder, W. S.: Textbook of Ophthalmology, St. Louis, Mosby, 1952, v. 5, p. 5202.
11. Erickson, O. F., Hatlen, R., and Berg, M.: Lacrimal proteins in correlation with the Schirmer test. Am. J. Ophth., **46**:12 (July Pt. II) 1958.
12. Friedman, B., and Gernand, O.: Sjoegren's syndrome treated with stilbestrol. Calif. & Western Med., **64**:31, 1946.
13. Gifford, S. R., Puntenney, I., and Bellows, J.: Keratoconjunctivitis sicca. Arch. Ophth., **30**:207, 1943.
14. Henderson, J. W., and Prough, W. A.: Influence of age and sex on flow tears. Arch. Ophth., **43**: 224, 1950.
15. Klein, M.: The lacrimal strip and the precorneal film in cases of Sjoegren's syndrome. Brit. J. Ophth., **33**:387, 1949.
16. Schirmer, O.: Student zur Physiol ɡie und Pathologie der Traenenabsonderung und Traenenabfuhr. Arch. f. Ophth., **56**:197, 1903.
17. Sjoegren, H.: Zur Kenntnis der Keratoconjunctivities Sicca, Acta Ophth. (Suppl. 2), **11**:1, 1933.

Opthalmic Miniature

Copley hesitated, and dropped his eyes. "Astigmatism, you know," he said, "is a defect—I quote the dictionary, I learned that definition by heart; I often puzzle over it still—causing images of lines having a certain direction to be indistinctly seen, while those of lines transverse to the former are distinctly seen.' Only mine is peculiar in the fact that my sight is perfectly normal except when I look back at anyone over my shoulder."

J. D. Beresford, *The Misanthrope*, 1918.

AMERICAN JOURNAL OF OPHTHALMOLOGY

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WILMER MEETING

The 20th clinical meeting of the Wilmer Residents Association was held at The Johns Hopkins Hospital in Baltimore on March 23rd, 24th, and 25th. The Residents Association is composed of former house officers and fellows of the Wilmer Ophthalmological Institute of The Johns Hopkins Hospital. Their annual clinical meeting provides an opportunity to review the work done in the Wilmer Institute during the past year and to follow the activities of members of the association. It has been the custom to invite a number of ophthalmologists from other cities to attend these meetings.

During the three-day meeting 420 members and guests were registered and a record

38 papers were presented. Dr. Maurice Langham's research laboratories were open for inspection and a number of research demonstrations were shown. Dr. Ronald Wood had an exhibit on sterile tonometry and Dr. Louise Sloan had an exhibit on basic reading aids. The completely remodeled out-patient clinic in the Wilmer basement was of special interest to all former Wilmer house staff.

From the first paper on Thursday morning "Technique and results of surgical removal of epithelial downgrowth," by A. Edward Maumenee, professor of ophthalmology and director of the Wilmer Ophthalmological Institute, to the final neuro-ophthalmological clinic conducted by Frank B. Walsh, professor of ophthalmology, the audience was treated to a variety of clinical and nonclinical ophthalmologic material. All essayists were kept honest as usual by the presence and comments of Frederick Verhoeff and vice versa.

The now traditional oyster roast supper on Thursday evening provided relaxation and an abundance of Chesapeake Bay delicacies. Dr. Shepard Dunn of Columbia, South Carolina, again won the prize for consuming the most oysters. The evening ended for some with a humorous phantasy put on by the Wilmer House staff.

The exciting plans for a new research building for the Wilmer Ophthalmological Institute were announced at the meeting and support for the project was enlisted from members of the Residents Association. It was also announced that the 1962 meeting will be held in Baltimore on April 12th, 13th and 14th.

PROGRAM

"Technique and results of surgical removal of epithelial downgrowth," A. Edward Maumenee; "Electromyographic studies of extraocular muscles: Normal and diseased," Marvin Sears and R. D. Teasdall; "Anion transport," Bernard Becker; "Postcontusion recession of iris angle and secondary glaucoma," Lorenz E. Zimmerman and Stewart M. Wolff; "Home tonometry," A. Edward Maumenee and Lane Reeves; "Candidiasis retinae," John M. McLean; "Observations concerning acid mucopolysaccharides in the trabecular meshwork of the chamber angle," James R. Duke and Sylvia Siegelman; "Ocular signs following stereotactic lesions of the thalamus and globus pallidus," J. Lawton Smith.

"Some observations on Purtscher's disease: Traumatic retinal angiopathy," William G. Marr; "Pigmentary glaucoma," Malcolm W. Bick; "Glaucoma after luetic interstitial keratitis," David L. Knox; "The use of sympathomimetic amines in the treatment of glaucoma," Angus L. MacLean; "Sterile tonometry," Ronald M. Wood; "Combined EENT approach to dacryostenosis," Richard E. Hoover and Alvin P. Wenger; "Combined EENT approach to orbital floor fractures," J. Willard Abrahams and Richard W. Dodd; "Useful variations in techniques for surgery of blepharoptosis," Robert A. Schimek; "Clinico-pathologic aspects of angioid streaks," David Paton.

"An improved method to preserve cytologic structure in histologic sections," Henry E. Wahlen and C. D. Dukes; "The syndrome of chronic keratoconjunctivitis, monoliasis, idiopathic hypoparathyroidism and Addison's disease," J. Donald M. Gass; "Contact lenses: Report of 300 cases," Charles Iliff, Howard Naquin and Pauline Long; "Focusable stand magnifiers," Louise L. Sloan; "The present status of the human electroretinogram," A. D. Ruedemann, Jr.; "Ophthalmodynamometry before and after endarterectomy," Stewart M. Wolff and Frank C. Spencer; "Mushroom corneal transplant," Charles W. Tillett; "Retinoblastoma among the offspring of adult survivors," P. Thomas Manchester.

"Studies on corneal deturgescence using intralamellar discs," Irvin P. Pollack; "Local tissue hypersensitivity reactions following injection of antigen into the cornea of normal rabbits," Lawrence B. Senterfit, Frederick G. Germuth, Jr., George E. McKinnon, and

Ernest W. Franklin, III; "New techniques in the histochemistry of the retina," Arnall Patz, Joseph Berkow, and Sara Rogers; "The effect of aqueous humor drainage on intraocular pressure," Carl Kupfer; "The effect of the Trendelenberg position on scleral rigidity and tonometry," Robert Moses.

"The influence of vascular changes on the pressure volume relationships in animal eyes," John E. Eisenlohr and Maurice E. Langham; "The reaction of the eye to the vascular changes following unilateral ligation of the common carotid artery," William J. Casey, II, and Maurice E. Langham; "The effect of pressure on ocular rigidity in living and enucleated human eyes studied manometrically," John E. Eisenlohr, Maurice E. Langham and A. Edward Maumenee.

"Palatal myoclonus," William A. Britton; "Epidural and subdural hematoma," John W. Pemberton; "Aseptic thrombosis of the cavernous sinus," Alfred McKinna and Frank B. Walsh; "Lesions of the optic tract," Richard Lindenberg; "Abnormal eye movements in a case of myasthenia gravis," Frank B. Walsh and David Knox; "Neuro-ophthalmology clinic," Frank B. Walsh.

Howard Naquin.

CORRESPONDENCE

Ophthalmic library wanted

Editor,

American Journal of Ophthalmology:

As secretary of the Detroit Receiving Hospital Alumni Association, I have been empowered to look for an ophthalmologic library consisting primarily of early ophthalmologic texts and ophthalmologic books of historical value to form the nucleus of a library which is to be started in honor of A. D. Ruedemann, Sr., M.D. I wonder if an announcement in The American Journal of Ophthalmology might put me in contact with an ophthalmologist who has such a collection for sale. I would be very grateful for any help in this matter.

(Signed) Leonard H. Lerner, M.D.
7310 West Seven Mile Road
Detroit 21, Michigan.

Retrobulbar Anesthesia

Editor,

American Journal of Ophthalmology:

The Gifford Memorial Lecture by Atkinson, which appeared in the January, 1961, issue of The Journal, recapitulates his important contributions to ophthalmic anesthesia. There are, however, points through which the ideas expressed can be carried further with profit.

In retrobulbar injection, to depend on a sedated patient to maintain a specific direction of gaze during the injection, is to accept the risk of an uncontrolled cutting instrument free in the muscle cone. This danger can be eliminated by grasping the external rectus fibers with either a plain or toothed forceps, moving the eye to the optimum position for injection and holding it firmly until the injection is completed. This means that every injection is exactly where the operator desires and the veins and other structures are not subjected to sudden trauma from unexpected ocular movements.

This small but important bit of technique was for me an outgrowth of an alteration in my muscle surgery anesthesia procedure. On the basis of changes in cardiac rhythm which can be produced by tension on extraocular muscles especially in anoxemia and following the publication of the work of Rhode, et al., in 1958 in The Journal, I instituted the routine use of retrobulbar anesthesia in addition to general anesthesia in all muscle surgery. Since this can be accomplished only by holding the eye with a forceps, I saw the advantage of doing the same thing in the cases in which local anesthesia was used.

I may add that I have had no technical

difficulty in the subsequent muscle surgery, including that on the four vertical muscles, or harmful effects from the use of retrobulbar anesthesia in general anesthesia. Even the minor disadvantage of a large pupil after the injection is neutralized in the monocular operations by leaving the other eye uncovered for observation. The anesthetists with whom I work have been enthusiastic about the results of retrobulbar anesthesia in minimizing the risk from cardiac irregularities and possible arrest, as well as reducing the total amount of the general anesthetic agent.

It is most unusual for cataract surgery to require general anesthesia. However, when indicated, the retrobulbar and seventh nerve blocks can be used as an adjunct with all the advantages so ably described in the Gifford Memorial Lecture.

In summary, I believe that ocular fixation by the operator is important in all retrobulbar anesthesia, that retrobulbar anesthesia should be regularly used in muscle surgery done under general anesthesia, and that in the rare case in which cataract surgery is done under general anesthesia, seventh nerve block and retrobulbar anesthesia should also be used irrespective of the agent used for the general anesthesia.

(Signed) Philip H. Landers, M.D.
Binghamton, New York.

BOOK REVIEWS

HIGHLIGHTS OF OPHTHALMOLOGY, 1960. By Benjamin F. Boyd, M.D. Panama, R.P., Starr & Herald Press, 1960. 312 pages, 115 illustrations, index. Price: Not listed.

We have come to recognize that *Highlights of Ophthalmology* by Benjamin F. Boyd is an essential and integral part of our current ophthalmic information. We all would be much poorer and inefficient without recourse to this modern, unique and delightful source of clinical ophthalmology.

I find it hard to catalogue or classify this work. It is not a journal, or a textbook, or an atlas, or a monograph, or a tear sheet, or a professional gossip column, or a scientific dialogue, or a "trade" periodical, or a do-it-yourself manual. It most skilfully combines all these factors, in fluent and well-edited English and illustrated with most excellently executed line drawings.

The present volume is rich with timely surgical topics and consists of detailed discussions of instrumentation, new developments in the operating room, laboratory care of eyebank eyes, treatment of iris melanoma, an excellent symposium on the effects of ionizing radiation and radiotherapy on ocular lesions, plastic and reconstructive surgery, and advances in cataract surgery, especially the use of alpha chymotrypsin in cataract surgery.

In addition there are two charming personal interviews, one between the author and Meyer-Schwickerath on "Light coagulation," and a chilling one with 10 Russian professors of ophthalmology, in which the author delineates his difficulties and persistence in fulfilling his self-imposed assignment. He points out the great contrast between the official blockage on the part of the bureaucratic state officials and the friendly and informative interview that finally resulted. In overcoming this short-sighted, stupid and block-headed barrier put up by the state officials, Drs. Boyd and Maumenee showed great patience and courteous persistence. It seems incredible to us in our free world that such a barrier to the exchange of information of great importance to all peoples should even have been considered. It supports the belief that "liberalism" and bureaucracy are the first refuge of the scoundrel.

The book concludes with a chapter of notes on the latest developments in ophthalmology. The authors of the various chapters are, H. M. Katzin, M.D., A. B. Reese, M.D., G. Cleasby, M.D., B. F. Boyd, M.D., Irene Hughes, B.A., A. W. Forrest, M.D., J.

McDonald, M.D., Fred Wilson, M.D., W. F. Hughes, M.D., Byron Smith, M.D., R. Troutman, M.D., Ramon Castroviejo, M.D., A. E. Maumenee, M.D., and John M. McLean, M.D.

If every ophthalmologist does not, as yet, know and use *Highlights,* he is missing the boat.

Derrick Vail.

AUDIO-HIGHLIGHTS OF OPHTHALMOLOGY. By Benjamin F. Boyd, M.D. Box 1189, Panama, Republic of Panama, 1960-1961 series. 12 one-hour tape recordings in total. Suitable for either (specified) 3¾ speed (large recorders) or 1⅞ speed (small recorders). Price: $57.00.

To any ophthalmologist who owns a tape recorder adjusted to either of these speeds, these tape-recordings bring lively discussions of up-to-date ophthalmic subjects. The mellow voice of Dr. Boyd in impeccable English, and beautifully edited, recites to you in your office, study, or in your car or on the train, even on the beach, the whys, wherefores, whos and whats of thoughts on all facets of ophthalmology. The opinions of world authorities are relayed to your ears and brains and can be listened to over and over by the individual or by groups around a table, a clever and most useful modern idea of teaching.

The success of these recordings are attested to by the fact that in the short time since their introduction, more than 600 subscriptions are in force.

Each department of ophthalmology in university and hospital should own a suitable tape recorder and subscribe to *Audio-Highlights of Ophthalmology* for use by its staff and residents.

Derrick Vail.

OPHTHALMOLOGY: A TEXTBOOK FOR STUDENTS AND PRACTITIONERS. By F. Rintelen, M.D. Basel, S. Karger Verlag, 1961. 455 pages, 124 illustrations in black and white, 38 color plates. Available in U.S.A. from Albert J. Phiebig, P.O. Box 352, White Plains, New York. Price: $18.00.

Rinetelen who occupies the chair of ophthalmology at the University of Basel, addresses his textbook to the medical student and the nonophthalmologist in the practice of medicine. It would seem that he has been singularly successful in his endeavors. The medical student will find a thorough and systematic presentation not only of the clinical material but also of the essential anatomic and physiologic facts of the eye and its adnexa. The general practitioner will be guided in the diagnosis of diseases and injuries of the eye which he is expected to recognize and to treat. Both should profit from the exhaustive discussion of ocular manifestations in systemic diseases. Even the ophthalmologist will gain useful information from perusal of this volume. I wonder how many of them are familiar with the *maladie des griffes de chat,* a lymphadenitis following scratch wounds caused by cats.

The arrangement of the book, quite naturally, follows more or less that of similar older examples. Of particular excellence are the chapters on the lacrimal apparatus and on extraocular motorics. There is also a very detailed description of the ophthalmoscopic aspects of arteriosclerotic and hypertensive retinopathy. Ophthalmologists will benefit from the lucid presentation of blepharospasm due to involvement of the extrapyramidal system.

A chapter on medico legal aspects and compensation with regard to ocular injuries is of interest to the Swiss physician only. Yet one cannot help but express a desire to see a similar unequivocal treatment of this subject in American textbooks and its application in court procedures. According to Swiss law, the mere possibility of a causal relation-

ship between an eye disease and an accident is not recognized as a warrant for compensation. This prevents undeserved and costly awards.

The discussion on glaucoma is perhaps a little disappointing. The mechanics of aqueous production and circulation are treated quite adequately. There seems to be not sufficient stress on the essential difference between open-angle and closed-angle glaucoma. At times, one actually gains the impression that the author himself does not believe in this difference, as for instance in his discussion of the various provocative tests. He states that megalocornea should always arouse suspicion of a congenital glaucoma; from the text it is not clear whether he means to say that megalocornea may be associated with glaucoma (a statement which obviously would be wrong) or whether it must be differentiated from hydrophthalmos. His choice of surgical treatment for acute glaucoma is the classical complete iridectomy rather than the more conservative yet equally effective basal iridectomy. Rintelen still adheres to the older idea of desquamation of the lens capsule as the cause of glaucoma capsulare in spite of the recent investigations by Theobald and Kirk and by H. Gifford.

The fluid style and lucid presentation maintained throughout are a joy. The illustrations and their reproductions are among the very best.

Stefan Van Wien.

THE EYE AND VIRUS. By R. Nataf, P. Lépine and G. Bonamour. Paris, Masson et Cie, 1960. 1022 pages, 172 figures, 20 plates of which 17 are in color. Price: Not listed.

In this superb monograph the authors discuss the ocular viruses and the ocular manifestations of general affections of viral origin from every point of view which could possibly interest the ophthalmologist. The discussions are exhaustive but not exhausting as one might think when he sees that they cover more than one thousand pages. The book is divided into four major parts.

In Part I the subject of general virology is discussed in 17 chapters. The authors make clear what a virus is. They describe its characteristics in general, its morphology and culture, its effects on the living cell, and the role of nucleoproteins in the chemical nature of the virus. In a second segment of this part they discuss the position of the virus in ocular pathology.

In Part II the authors provide a systematic discussion on the role of viral infection in each anatomic segment of the eye—the lids, conjunctiva, sclera, lacrimal organs, the cornea, the uvea, the optic nerve, the motor system, the retina, and in the embryopathies.

In Part III the ophthalmologic manifestations in the course of general viral diseases are discussed.

Part IV is devoted to syndromes which are actually accepted as viral in nature. In the first of the three chapters in this segment the authors discuss the pluri-orificial ectodermoses, namely, (1) Reiter's syndrome, (2) Stevens-Johnson disease, pemphigus, (3) the varicelliform eruption of Kaposi, and (4) the aphthoses. The subject of a second chapter is the malady of Behçet-Adamatiades, and in the third chapter the accumulated knowledge of the uveomeningeal syndrome is presented. In a final very brief segement entitled "By way of conclusion," general viral affections are reviewed.

These statements provide only a suggestion of the enormous range of the authors' discussion but cannot convey my enthusiastic admiration of this excellent monograph.

F. HERBERT HAESSLER

ABSTRACT DEPARTMENT

EDITED BY DR. F. HERBERT HAESSLER

Abstracts are classified under the divisions listed below. It must be remembered that any given paper may belong to several divisions of ophthalmology, although here it is mentioned only in one. Not all of the headings will necessarily be found in any one issue of the Journal.

CLASSIFICATION

1. Anatomy, embryology, and comparative ophthalmology
2. General pathology, bacteriology, immunology
3. Vegetative physiology, biochemistry, pharmacology, toxicology
4. Physiologic optics, refraction, color vision
5. Diagnosis and therapy
6. Ocular motility
7. Conjunctiva, cornea, sclera
8. Uvea, sympathetic disease, aqueous
9. Glaucoma and ocular tension
10. Crystalline lens
11. Retina and vitreous
12. Optic nerve and chiasm
13. Neuro-ophthalmology
14. Eyeball, orbit, sinuses
15. Eyelids, lacrimal apparatus
16. Tumors
17. Injuries
18. Systemic disease and parasites
19. Congenital deformities, heredity
20. Hygiene, sociology, education, and history

6

OCULAR MOTILITY

Cristini, G. **The syndrome of agnosis in concomitant strabismus.** Riv. oto-neuro-oftal. **35**:349-362, July-Aug., 1960.

The author presents a review of the literature concerning the various sensory-motor disturbances that occur in patients with concomitant strabismus. He also presents his own theories concerning the mechanism of agnosia in such strabismus.

Wm. C. Caccamise.

Herzau, W. **Horror fusionis and convergence excess in anisometropia and aniseikonia.** Klin. Monatsbl. f. Augenh. **137**: 781-785, 1960.

Anisometropia and aniseikonia combined with convergent and vertical strabismus with horror fusionis were present in an 18-year-old student. Fixation at near resulted in marked convergence excess of the non-fixating eye. By optical correction of the refractive error and the use of an aniseikonic lens the horror fusionis was broken and the eyes became parallel for distance. The convergence excess at near was corrected by reducing the accommodative effort with spherical lenses. (5 figures, 4 references)

Gunter K. von Noorden.

Holland, G. **Binocular vision and anomalous retinal correspondence in small angle squint.** Klin. Monatsbl. f. Augenh. **137**:786-797, 1960.

Thirty-five patients with small-angle esotropia and harmonious ARC were examined as to their binocularity. Five patients had alternating esotropia. Nonfoveal fixation was present in five out of the remaining 30 patients. The average angle of anomaly was 6.3 degrees. Amblyopia ranged from 5/7 to 1/10. Binocularity was tested on the synoptophore, the stereo-eidometer (Monjé), and by the Worth test. The average fusional amplitude ranged from +10 degrees to −6 degrees. The Worth test was positive (i.e. all four dots were seen) in all patients at a distance of 1 meter. However, suppression prevailed at greater distances with this test, particularly in patients with larger angles of anomaly. The author emphasizes in patients with monocular amblyopia and apparently straight eyes, small-angle squint with harmonious ARC, may be present. (2 tables, 24 references)

Gunter K. von Noorden.

Hollwich, F. **The limitations of surgical procedures in convergent squint.** Klin. Monatsbl. f. Augenh. **137**:729-736, 1960.

The analysis of the motility of the horizontal eye muscles reveals a wide range of movement of the individual muscle. Advantages and disadvantages of a combined recession and resection are discussed. The aim of surgery is not only elimination of the deviation, but also restoration of sufficient motility. A rigid scheme indicating the amount of surgery to be done for each degree of deviation cannot be given. However, it is desirable to be able to refer to approximate values when planning the surgical procedure. Such values are given. Frequently the forced duction test (Scobee) yields information as to the type of surgery to be done. (3 figures, 33 references)

Gunter K. von Noorden.

Jonkers, G. H. **The indications for pleoptic and orthoptic treatment.** Klin. Monatsbl. f. Augenh. **137**:145-155, 1960.

The author discusses and critically evaluates the various forms of therapy for amblyopia in convergent and divergent strabismus. He refers briefly to the possibilities and limits of binocular training and notes the degree of therapeutic success in the various forms of disturbance of motor and sensory equilibrium. (7 references) F. H. Haessler.

Kerrinnes, E. **Pseudoparesis of the inferior oblique muscle (sheath syndrome).** Klin. Monatsbl. f. Augenh. **137**:741-747, 1960.

The literature on the superior oblique tendon sheath syndrome (Brown) is reviewed. One case of pseudoparesis of the inferior oblique of the right eye is reported. A traction test under anesthesia was positive; the eye could not be rotated above the horizontal with forceps. The differential diagnosis between apparent and genuine paresis of the inferior oblique muscle is discussed. (1 figure, 29 references) Gunter K. von Noorden.

Kitamuro, T. **Measurement of total myodiopters by Maddox-rods.** Acta Soc. Ophth. Japan **64**:2485-2510, Oct., 1960.

In the first part of this attempt to employ Maddox rods in measurement of total myodiopters according to the Mitsui-Fukushima principle the author studied the behaviour of convergence due to the proximal factor (C.P.F.). He measured the C.P.F. and accommodative convergence (A.C.) as follows. The convergence measured by the Maddox test at the distance of 33 cm. represents the sum of A.C. for 3.0 diopters and C.P.F. for 33 cm. The convergence measured similarly after applying a +3.0 D lens on each eye represents C.P.F. for 33 cm. The difference between the two measurements represents the actual A.C. for 3.0 D. When homatropine was instilled into the eye it caused an increase of accommodative convergence in proportion to the advance of accommodative paresis as indicated by Mitsui-Fukushima. Nevertheless, the C.P.F. remained unchanged. Thus he concluded that the C.P.F. was not dependent on A.C.

In the second part of his study the author measured the total myodiopter by means of the Maddox test. The total myodiopters were calculated by the following formula:

$$\text{T.M.D.} = 3.0\ \text{D} \times \frac{\text{A.C.}_2}{\text{A.C.}_1}$$

where A.C._1 is actual accommodative convergence for 3.0 D. before homatropine is instilled and A.C._2 is that taken after the near point has retroceded to 33 cm. because of the instillation of homatropine. (43 figures, 4 tables, 8 references)

Yukihiko Mitsui.

Landgraf, S. **Functional results with muscle grafting in sixth nerve paralysis.** Klin. Monatsbl. f. Augenh. **137**:737-741, 1960.

The functional results obtained with the

Hummelsheim procedure (modified after O'Connor) were improved by orthoptic exercises in three cases. (9 figures, 16 references) Gunter K. von Noorden.

Mosquera, J. M. **Television in the treatment of some forms of diplopia.** Arch. oftal. Buenos Aires **35**:319-322, Sept., 1960.

On the basis of a somewhat scant material (two cases of slight paresis, and two of complete paralysis of one external rectus muscle, of which the latter showed no demonstrable improvement), the author claims that a substantial progress may be achieved by having patients who have diplopia watch a television screen through prisms of adequate power. One does not very well see why this should occur under the conditions stated rather than with the aid of a simpler device which consists of looking at a busy street scene through a window pane of adequate size. A. Urrets-Zavalía, Jr.

Papst, W. and Essler, E. **The etiology of congenital abducens paralysis.** Klin. Monatsbl. f. Augenh. **137**:306-327, 1960.

Electromyographic studies revealed a hitherto unrecognized central disturbance of innervation. The disturbance of the paradoxic innervation and synergistic action of the two horizontally-acting extraocular muscles is analyzed in great detail. (11 figures, 2 tables, 26 references) F. H. Haessler.

Piper, H. F. and von Volkman, U. **Phenomenons of localization in strabismic amblyopia.** Klin. Monatsbl. f. Augenh. **137**:798-807, 1960.

The behavior of the subjective vertical and horizontal was investigated in 25 amblyopic patients. The results were compared with the sound eye of the same subject. In most instances the subjective vertical of one eye appeared to be in an inclined position, which was opposite to the direction of head inclination during the test ("E-phenomenon"). The other eye localized approximately according to the objective position of the illuminated line which was employed for the experiment. In another test 20 patients estimated incorrectly the point of bipartition of a straight horizontal line. In 18 of these patients Kund's type of bipartition prevailed in the sound eye and Münsterberg's type of bipartition was encountered in the amblyopic eye. (2 figures, 1 table, 56 references) Gunter K. von Noorden.

Richter, Susanne. **The results of pleoptic and orthoptic treatment.** Klin. Monatsbl. f. Augenh. **137**:155-160, 1960.

The author summarizes her experience in pleoptic and orthoptic treatment of 683 children, aged five to 12 years, who had strabismus. They were observed for a period of one to three years. Therapy was definitely successful in children who had central fixation from the beginning; this was the case in one sixth of the patients. In alternating squint therapeutic results were very good in one fifth of the children. (1 figure) F. H. Haessler.

7

CONJUNCTIVA, CORNEA, SCLERA

Franceschetti, A. and Thier, C. J. **Corneal dystrophies in genodermatoses with particular regard to planoplantar keratoses.** Arch. f. Ophth. **162**:610-670, 1961.

Genodermatosis denotes any hereditary systemic malady of the skin. Secondary corneal affections occur when the lid margin or conjunctiva become involved, yet primary corneal dystrophies have been little known. Their description and classification is here based upon clinical, histologic and genetic features, which are elucidated by means of case reports and many illustrations.

In one group corneal changes are always associated with the dermatosis,

which has a well defined and mostly recessive hereditary pattern. Included are: epideromlysis bullosa polydystrophica, keratosis palmoplantaris and keratosis follicularis spinulosa declavans. In the other group corneal dystrophies are seldom seen and the genetic pattern is ill defined (ichthyosis vulgaris, infantile poikilodermia (Rothmund), pityriasis rubra pilaris, keratosis follicularis (Darier-White), anhidrotic form of ectodermal dysplasia, and angiokeratoma corporis diffusum of Fabry). (32 figures, 164 references. Harri H. Markiewitz.

Glasmacher, Helmuth. **Experimental studies of the corneal lime burn and its therapy.** Arch. f. Ophth. **162**:493-499, 1960.

Corneas of freshly enucleated cattle eyes were submitted to controlled action of lime. Calcium concentration was then measured before and after the corneas were respectively treated with water, acetic acid, hydrochloric acid, ascorbic acid or ethylenediamine-tetraacetic acid (EDTA). The last substance was found most effective in removing the calcium. (3 figures, 1 table, 11 references)

Harri H. Markiewitz.

Kitano, S., Liu, J., Ochi, N. and Takemura, T. **Effect of topical corticosteroids in experimental herpetic keratitis in rabbits.** Acta Soc. Ophth. Japan **64**:1990-2004, Aug., 1960.

By a topical application of corticosteroids the incubation period of experimental herpetic keratitis is shortened in 44 percent of rabbits and the keratitis is apt to be severe in 60 percent. Encephalitis is brought about in 50 percent of the cases. These effects of corticosteroids appear only by an application after inoculation or during the appearance of keratitis. An application before inoculation and that after cure of keratitis show little effect. (8 figures, 6 tables, 47 references)

Yukihiko Mitsui.

Klemens, Fritz. **Indications for lamellating keratoplasty.** Klin. Monatsbl. f. Augenh. **137**:43-49, 1960.

The author reports his experience with lamellating keratoplasty in four patients with severe destructive corneal lesions which had resisted all conservative therapy. In all of the patients lamellating keratoplasty was followed by improvement. The pertinent literature is reviewed. (8 references) F. H. Haessler.

Kreibig, W. **Bowen's disease and the eye.** Klin. Monatsbl. f. Augenh. **137**:721-728, 1960.

The histologic characteristics of Bowen's disease are discussed. Two cases are reported. The eye had to be enucleated in one patient; the conjunctival tumor was excised in the second. However, the lesion recurred after three months and could be treated successfully by subconjunctival injections with a cytostatic drug (Bayer E 39). (5 figures, 12 references)

Gunter K. von Noorden.

Kwedar, E. W. **Hereditary nonprogressive deep corneal dystrophy.** A.M.A. Arch. Ophth. **65**:127-129, Jan., 1961.

Two cases in relatives are reported. The lesions were nodular and limited to Descemet's membrane and the endothelium. They seemed evenly distributed over the posterior cornea. Vision was normal in one man but could not be corrected over 20/40 in his son. (2 figures, 3 references)

Edward U. Murphy.

Lassmann, G. **The innervation of the cornea.** Arch. f. Ophth. **162**:565-609, 1961.

On the basis of the results of various histologic and histochemical examinations the nerve fibers in the rabbit's cornea may be grouped into four main kinds of plexus, one each for the endothelium, the epithelium, and the deep and superficial stromal layers. The fibers are cholinesterase-positive, seem to be of sensible

nature and posses a sheath. In the stroma they end intra- and extracellularly in the form of the metaterminal apparatus of Weber. Sympathetic innervation seems to exist in the vascular limbus normally and in the stroma after inflammatory neovascularization. Parasympathetic pathways could not be clearly shown. In the stroma the relationship of the corneal cells to the nervous elements is distinct from the picture in undifferentiated connective tissue. (39 figures, 123 references)

Harri H. Markiewitz.

Marquardt, Rolf. **The course and therapy of corneal aspergillosis with antibiotics and corticoids.** Klin. Monatsbl. f. Augenh. **137**:211-217, 1960.

The author reports a case of ulcerative corneal aspergillosis with progredient course in spite of preliminary antibiotic and corticoid therapy, in which subsidence of the fungus infection could be achieved by means of a penetrating keratoplasty. With reference to bibliography the author discusses the increasing frequency and malignancy of keratomycoses since the introduction of antibiotics and corticoids into ophthalmic therapy. (3 figures, 17 references) Author's summary.

Molnár, L., Herpay, Z. and Gát, G. **Conjunctival mycosis caused by Cephalosporium niveolanosum (Benedek).** Arch. f. Ophth. **162**:486-492, 1960.

A rare case of primary mycotic infection is presented in its mycologic and therapeutic aspects. (5 figures, 15 references) Harri H. Markiewitz.

Oglesby, R. B. **Corneal opacities in a patient with cryoglobulinemia and reticulohistiocytosis.** A.M.A. Arch. Ophth. **65**: 63-66, Jan., 1961.

The lesions were located peripherally in the posterior stroma and Descemet's membrane. The pupillary area was spared and vision was normal. (1 figure, 15 references) Edward U. Murphy.

Payrau, P. **Preservation of corneal tissue and heteroplasty.** Klin. Monatsbl. f. Augenh. **137**:49-55, 1960.

Experience with more than 100 experimental heteroplasties and in 20 clinical cases has convinced the author that corneas which have been lyophilized or desiccated by the application of silica gel may be stored for several months. With the help of the procedures described by the author it is now possible to organize eye banks. He has also shown that the corneas of an animal's eye may be successfully transplanted to the human eye. (2 figures, 15 references)

F. H. Haessler.

Remky, H. **First experimental and clinical experiences with the use of preserved corneas.** Klin. Monatsbl. f. Augenh. **137**: 56-60, 1960.

By the use of the method designed by P. Pəyrau (which consists of silico-desiccation after preliminary deep freezing) one can prepare corneal tissue so that it can be kept at room temperature for months without structural change, be germ-free, and will have hardly any antigenic properties. The author reports in detail his chemical and physical studies of such preserved corneas, and observations on animal experiments on transplantation of such tissue in keratoplasties. (4 figures, 1 table, 3 references) F. H. Haessler.

Roveda, J. M. and Blumenkrantz, N. **The toluidine blue microtest in viral diseases of the cornea and conjunctiva.** Arch. oftal. Buenos Aires **35**:307-309, Sept., 1960.

When the conjunctival secretion which is taken from eyes with one of several external, supposedly viral conditions is suspended in a drop of distilled water to which a drop of 0.1 percent toluidine blue is added, a fibrilar precipitate, colored

purple instead of blue, (metachromasia) may be observed under the microscope. This reaction, which is related to that encountered in cases of vernal catarrh, seems due to the presence of a highly polymerized, acid mucopolysaccharide in the material studied. (6 figures, 3 references) A. Urrets-Zavalía, Jr.

Sivasubramaniam, P. and Mutucumarana, D. **Scleromalacia perforans.** Brit. J. Ophth. **44**:765-767, Dec., 1960.

A case of bilateral intercalary staphyloma is presented. The ectasia was in the superior nasal quadrant. The cornea was vascular. No cholesterolemia or joint involvement was present. (2 figures, 6 references) I. E. Gaynon.

Sugiura, S. and Wakui, K. **Block structure of corneal epithelium with special reference to the development mechanism of dendritic keratitis.** Acta Soc. Ophth. Japan **64**:1879-1887, Aug., 1960.

When the virus of herpes simplex is inoculated into the rabbit's cornea, a herpetic keratitis results. This keratitis is manifest as a row of nodules. The nodules are arranged regularly at intervals of 0.36 mm. on the average. The nodules are connected with a delicate canal to make a rosary. A channel may turn or several channels may unite at one nodule. Inside a nodule radiating channels are found. From these findings the authors consider that a block structure is present in the corneal epithelium; namely, the epithelial layer is divided into small blocks of 0.3 to 0.4 mm. in diameter by channels. The herpes virus produces nodular lesions at the intersections of the channels and spreads through the channel to reach the next intersection, thus to form a dendritic appearance. The rosary appearance of superficial keratitis can also be observed in a vaccinia keratitis and a chemical keratitis due to croton oil, though the appearance is not lasting and is not so impressive as in cases of herpetic keratitis. (15 figures, 6 references) Yukihiko Mitsui.

Thomas, C. I. **Annual reviews. Cornea and sclera.** A. M. A. Arch. Ophth. **65**: 243-317, Feb., 1961.

The literature from September, 1959, to September, 1960, is reviewed. (337 references) Edward U. Murphy.

8

UVEA, SYMPATHETIC DISEASE, AQUEOUS

Donaldson, D. D. **The significance of spotting of the iris in mongoloids.** A. M. A. Arch. Ophth. **65**:26-31, Jan., 1961.

The irides of 180 mongoloids and 157 normals were studied photographically. Brushfield's spots were found in 85 percent of the mongoloid and 24 percent of the normal individuals. In the mongoloid these spots are generally more distinct, more numerous, and usually located in the mid-zone of the iris. There is also an association of marked peripheral thinning of the iris. In the normal the spots are less distinct, less numerous, and situated in the periphery which is not unusually thin. Four eyes were also studied histologically. The most prominent feature was the marked hypoplasia of the peripheral iris. (14 figures, 9 references) Edward U. Murphy.

Pameyer, J. K. Waardenburg, P. J. and Henkes, H. E. **Choroideremia.** Brit. J. Ophth. **44**:724-738, Dec., 1960.

Choroideremia is a rare sex-linked abiotrophic process of the tapetum nigrum with a secondary progressive dystrophy of the choriocapillary layer and outer retinal layers which occurs in males. The disease leads to blindness.

Three patients and six carriers in two families are discussed. The visual fields, dark adaptation, color vision and electro-

retinographic findings are given. (10 figures, 1 pedigree, 15 references)

I. E. Gaynon.

Urayama, A., I. Ikeda, I. and Shikano, S. **Symposium: Uveitis.** Acta Soc. Ophth. Japan **64**:2263-2371, Sept., 1960. I. Urayama, A. **The etiology and pathogenesis of uveitis.** pp. 2263-2301. II. Ikeda, I. **Studies on the etiology of uveitis with special reference to stress.** pp. 2302-2340. III. Shikano, S. **A histopathological study on Behçet's disease.** pp. 2341-2371.

In the first part of this symposium on uveitis by three authors Urayama reports statistics of uveitis. During the past two years he saw 187 cases of uveitis and they were classified as follows: syphilis 4.2 percent, tuberculosis 9.5 percent, rheumatism 3.2 percent, leptospirosis 17.5 percent, sarcoidosis 3.7 percent, toxoplasmosis (?) 0.5 percent, Behçet's disease 14.3 percent, Vogt-Koyanagi-Harada's syndrome and sympathetic ophthalmia 5.8 percent, others of known origin 0.5 percent and unidentified origin 40.3 percent. He then discusses the method of identification. Behçet's disease often affects all of the systemic organs and his statistics of 53 cases show that the digestive system was affected in 11.3 percent of cases, the respiratory system in 7.5 percent, the circulatory system in 18.9 percent, and the central nerve system in 23.1 percent. (35 figures, 29 tables, 101 references)

The second author claims that a stress is important in the manifestation of uveitis as a disposing or provoking factor. (6 figures, 67 tables, 83 references)

The third author deals with the pathology of Behçet's disease. He concludes that Behcet's disease is one of the strictly defined collagen diseases characterized by a transient course of the attack and by strong hemorrhage and exudation in the lesion. (35 figures, 1 table, 17 references)

Yukihiko Mitsui.

9

GLAUCOMA AND OCULAR TENSION

Cramer, F. K. and Lamela, N. A. **Comparison of the intraocular pressure readings obtained with the applanation and the Schiøtz tonometers.** Arch. oftal. Buenos Aires **35**:261-267, July, 1960.

In 60 randomly selected and apparently normal eyes—on the refractive status of which no information is given—measurements of the intraocular pressure were made successively with Goldmann's applanation tonometer and with a certified Schiøtz tonometer. In the case of this latter, both single 5.5 gram plunger load readings, and paired readings with the 5.5 gm. and 10 gm. plunger loads were taken into account. As inordinately large differences were found between the estimates made with the applanation tonometer and those obtained with the 5.5 gm. plunger load on the Schiøtz tonometer (in 21 of the 60 reported eyes this discrepancy amounted to 4.5 mm. Hg or more, in 11 to 8 mm. or more, and in five to 11 mm. or more), which went much beyond the accepted range of error (cf. Armaly, M. F.: Schiøtz tonometer calibration and applanation tonometry, A.M.A. Arch. Ophth. 64:426-432, Sept., 1960), and as the readings were in the second case uniformly lower than in the former, it might be suspected that the calibration of at least one of the instruments used was altered. The fact that a better agreement between measurements was attained when paired readings were used with the Schiøtz tonometer, leads one to believe that this last was at fault. (1 graph, 4 tables, 11 references)

A. Urrets-Zavalía, Jr.

Gloster, J. **Responses of the intra-ocular pressure to diencephalic stimulation.** Brit. J. Ophth. **44**:649-664, Nov., 1960.

Since advance of the hypothesis of the presence of a center or centers in the diencephalon for the control of ocular

pressure, there has been much laboratory study of this subject with various conclusions, none of which have been completely acceptable. In this report the author describes in detail more such experiments in which different types of stimulation and different methods of observation were used; the results are described in detail. Anesthetized cats were used and the stimulation was accomplished by much smaller electrodes than had been used previously. In 35 cats 977 stimulations were applied and the various elevations and depressions of ocular pressure were recorded and are summarized. At times these changes were associated with the same changes in general blood pressure, at other times the opposite change in general blood pressure occurred and there were times when the changes in intraocular pressure were independent of any other changes.

The author concludes that these experiments failed to demonstrate the existence in the diencephalon of any areas or centers specifically concerned with regulation of the intraocular pressure and therefore the hypothesis of this arrangement should be rejected. (16 references)

Morris Kaplan.

Marg, Elwin, MacKay, R. S. and Oechsli, R. **Corneal bending and buckling in tonometry.** A.M.A. Arch. Ophth. **65**: 67-74, Jan., 1961.

A new tonometer is described and its principles are discussed. A variable inductance transducer with mechanical negative feedback is used to flatten the cornea momentarily and the restoring force needed to maintain the transducer surface co-planar with the surrounding region is recorded as a measure of the intraocular pressure. The authors claim that the errors inherent in other methods of tonometry are eliminated. They stress the fact that no local anesthesia is necessary. (7 figures, 5 references)

Edward U. Murphy.

Miyake, M. **A study of aqueous outflow by applanation tonometry.** Acta Soc. Ophth. Japan **64**:2557-2571, Oct., 1960.

In this study of ocular tension by means of an applanation tonometer the figure representing the ocular tension was slightly lower than that given by the Schiøtz tonometer. In primary glaucoma the ocular rigidity is always greater than that of normal eyes but not in secondary glaucoma. The ocular tension immediately after a compression test (50 gm. for 10 minutes) can not be measured by the Schiøtz tonometer in normal eyes but it can be measured by an applanation tonometer. (13 figures, 13 tables, 27 references)

Yukihiko Mitsui.

Mizukawa, T., Nakabayashi, M., Manabe, R., Otsuji, T. and Katano, T. **Flicker ERG in experimental glaucoma and influence of illumination.** Acta Soc. Ophth. Japan **64**:2205-2209, Sept., 1960.

An experimental glaucoma was produced in rabbits by employing an apparatus for manometry. Flicker ERG was measured in such rabbits. The critical fusion frequency (c.f.f.) as shown by ERG decreased rapidly with an increase in ocular tension. The recovery in the c.f.f. was delayed in proportion to the duration of the glaucomatous condition. The change in the c.f.f. was almost parallel with the decrease in the b- and c-waves of the ERG.

The recovery of the c-wave after cessation of the glaucomatous condition was then studied. When the eye was illuminated during the period of ERG disappearance by high ocular tension, the recovery of the c-wave was delayed very much. This fact indicates that dark and light adaptation can take place in the retina during the ischemia. (10 figures, 16 references)

Yukihiko Mitsui.

Scheie, H. G. **Goniopuncture: an evaluation after eleven years.** A.M.A. Arch. Ophth. **65**:38-48, Jan., 1961.

Goniotomy done as a primary procedure on 21 eyes with infantile glaucoma was successful in 62 percent of them. Goniopuncture showed success in 52 percent of 52 eyes. When both operations were combined and done on 117 eyes, 76 percent were controlled. In juvenile glaucoma goniopuncture normalized tension in 57 percent of the patients. In patients over 30 years of age this procedure seems to be ineffective, probably because of the reduction in elasticity of corneoscleral tissue with age. (6 figures, 3 tables, 8 references) Edward U. Murphy.

Suda, K., and Furushima, M. **A tonometer with a convex plunger.** Acta Soc. Ophth. Japan **63**:2445-2451, July, 1959.

The authors describe tests with a tonometer which has a convex plunger, the radius of convexity of which is 1.5 mm.; with it, it is possible to measure a considerably wider range of ocular pressure without changing the load. They feel that the convex plunger is considerably superior to the Schiøtz concave plunger or the McLean plane plunger. (4 figures, 11 references) Yukihiko Mitsui.

Thiel, R. **Secondary glaucoma after epithelial or endothelial invasion into the anterior chamber.** Klin. Monatsbl. f. Augenh. **137**:705-720, 1960.

The author differentiates between three types of iris cysts, the idiopathic, traumatic and secondary form on the basis of their origin, structure and localization. The idiopathic form includes cysts of the iris stroma or the pigment epithelium. Traumatic cysts occur after cataract or glaucoma surgery and may be the result of epithelial invasion, or caused by implantation of epithelial cells. Secondary iris cysts may be due to the continued use of miotics, to degenerative processes in older people, or they may be caused by inflammations of the iris, in which case they have exudative character. Tuberculomas, syphilomas, or melanomas of the iris must be considered in the differential diagnosis of iris cysts. Traumatic iris cysts frequently lead to complications, of which secondary glaucoma is the most severe. Various methods of treatment for iris cysts are discussed. The author prefers total excision of the cyst with complete iridectomy, and has recently begun to perform this procedure in two sessions. (16 figures, 82 references)

Gunter K. von Noorden.

10

CRYSTALLINE LENS

Barthelmess, G. **Vision with the anterior chamber lens. I. Monocular functions.** Arch. f. Ophth. **162**:527-544, 1960.

The optical problems of anterior chamber lenses are well reviewed and analyzed, with anisometropia of unilateral aphakia particularly in mind. The author describes 73 of 182 patients in whom implants were made by the method described by Schreck; in only four of them was full visual acuity achieved without further correction. (4 figures, 3 tables)

Harri H. Markiewitz.

Barthelmess, G. **Vision with the anterior chamber lens. II. Binocular functions.** Arch. f. Ophth. **162**:545-564, 1961.

Whereas visual acuity furnished a fair criterion to gauge monocular functions, the analysis of binocular vision met with many methodologic difficulties. To attain sound judgment six different methods were used in addition to standard tests of muscle balance. Of the 73 reported patients, whose unilateral aphakia was corrected by anterior chamber lens implants, eight achieved completely "normal" binocularity. Orthoptic exercises, time, and the great adaptability of the visual apparatus are some of the factors which facilitate restoration of binocular coordination. After a most extensive and thorough in-

vestigation it is concluded that on optical grounds the anterior chamber lens implant meets, and even surpasses, the expectations. (1 table, 51 references)
Harri H. Markiewitz.

Bessiere, E. and Pelegris, G. **Coexistent chronic noncongestive glaucoma and senile cataract: surgical treatment.** International College Surgeons **35**:77-82, Jan., 1961.

The authors' technique is as follows: a limbus-based conjunctival flap is made by the use of a Nicati knife in doing the corneo-scleral incision. Total iridectomy is then performed. A piece of sclera is resected with punch forceps, the incision is then enlarged with Castroviejo scissors, and the lens is removed intracapsularly if possible. Corneo-scleral sutures are placed at nine and three o'clock and the conjunctival flap is then sutured. (7 figures, 17 references) I. E. Gaynon.

Fechner, P. Ullrich. **The expression method for cataract surgery.** Klin. Monatsbl. f. Augenh. **137**:30-43, 1960.

The author describes a method of intracapsular cataract extraction which greatly reduces the danger of tearing of the capsule and vitreous complications. It is a method of expression with a smooth capsule forceps or erisophake. In a series of 127 planned intracapsular extractions the capsule ruptured, in six cases vitreous appeared in the anterior chamber and in three there was loss of vitreous. The procedure is contraindicated when there is damaged corneal endothelium, as in the corneal dystrophy of Fuchs or after perforating corneal transplantation. (5 figures, 4 tables, 36 references)
F. H. Haessler.

Gärtner, Jürgen. **On the course of the Roentgen cataract in the sympathectomized rabbit's eye.** Arch. f. Ophth. **162**: 471-485, 1960.

Cervical sympathectomy does not alter the development of cataracts produced by X-ray radiation. The possible etiologic causes of unilateral spontaneous cataracts are reviewed. (1 figure, 3 tables, 25 references Harri H. Markiewitz.

Hanno, H. A. and Weiss, D. I. **Pseudohypoparathyroidism.** A.M.A. Arch. Ophth. **65**:221-225, Feb., 1961.

Two patients, one 28 and the other 22 years of age, came under medical observation because of cataracts. Idiopathic hypoparathyroidism was the initial clinical impression in both cases but the demonstration of bony dysplasia by X-ray studies changed the diagnosis to pseudohypoparathyroidism. This condition is very rare but should be considered in younger patients who have cataracts. (4 figures, 8 references) Edward U. Murphy.

Hayano, S. **Three cases of anterior chamber lens implant.** Acta Soc. Ophth. Japan **64**:2043-2048, Sept., 1960.

In two of the three cases in which an anterior chamber lens was inserted after unilateral cataract surgery, good vision was obtained and, in one of them, binocular vision. The course was followed for six to 18 months. (7 figures, 2 tables, 10 references) Yukihiko Mitsui.

Jonkers. **Secondary glaucoma after lens extraction.** Klin. Monatsbl. f. Augenh. **137**:13-20, 1960.

The author feels that the best method for preventing the occurrence of secondary glaucoma after cataract extraction is to remove the lens intracapsularly and, when possible, to make radial iridotomies after which there will be a round pupil. The anterior chamber should be closed with corneo-scleral sutures and filled with normal saline solution. He recommends opening the chamber with lance and scissors. (12 references) F. H. Haessler.

Lerman, Sidney. **Carbohydrate metabolism in the rat lens as related to the age of the animal.** A.M.A. Arch. Ophth. **65**: 181-183, Feb., 1961.

Experiments with young and mature lenses indicate that there is an alteration in at least one metabolic pathway as the lens ages. This may be an important factor in determining the degree of susceptibility of the lens to the cataractogenic action of galactose and xylose. (2 tables, 8 references) Edward U. Murphy.

Müller, H. K. and Kleifeld, O. **The treatment of senile cataract with Debenal.** Klin. Monatsbl. f. Augenh. **137**:25-29, 1960.

The authors' observations gave no evidence that Debenal therapy influences the course of senile cataract but they point out that the number of their patients was too small and the time of observation too short to justify a statement that Debenal has no effect. (4 tables, 6 references) F. H. Haessler.

11

RETINA AND VITREOUS

Aoki, H., and Kamei, T. **The function of the mesencephalon in degeneratio pigmentosa retinae.** Acta Soc. Ophth. Japan **64**:2165-2173, Sept., 1960.

A water drinking test shows an increased diuresis in patients with pigmentary degeneration of the retina. The test is less influenced by oxytocin in patients than in normal controls but more influenced by thyradin. When calcium ions are given to the patients and controls a greater increase of the ion in the serum occurs in the serum of the patient than in that of the controls. When methionine is given to patients their blood glutathion is reduced more rapidly than that of the controls. A decrease of serum cholesterol by administration of sexual hormone is less pronounced in patients than in controls. (1 figure, 17 tables, 18 references) Yukihiko Mitsui.

Brandt, H. P. and Zenker, H. **Weather conditions and intraocular hemorrhages in periphlebitis retinae.** Klin. Monatsbl. f. Augenh. **137**:752-765, 1960.

The authors observed 286 recurrent hemorrhages during 3,287 days which were correlated statistically with the prevailing weather conditions recorded for each day. More than one-third of the hemorrhages occurred on days with particularly bad weather. The authors caution against over-evaluating the significance of this coincidence. It is pointed out, however, that the vegetative nervous system and certain reflex connections between diencephalon and eye (Thiel and Hollwich) may be influenced by meteriological conditions. (5 figures, 2 tables, 55 references) Gunter K. von Noorden.

Campbell, F. P. **Retinal vein occlusion.** A.M.A. Arch. Ophth. **65**:2-10. Jan., 1961.

The retinal light coagulator of Meyer-Schwickerath was used in experimental occlusion of the retinal vein in the cat. The fundus changes and microscopic findings are described. (8 figures, 9 references) Edward U. Murphy.

Correa, I. **Disciform macular degeneration.** Rev. brasil. oftal. **19**:275-292: Dec., 1960.

The author reviews the literature of disciform macular degeneration and believes it is of choroidal origin and situated in the submacular region. He presents two cases of the disease and reviews its three stages, distrophic, pseudotumoral and atrophic. He also reviews the important factors in the differential diagnosis and emphasizes the great importance of fundus biomicroscopy. (4 figures, 43 references) Walter Mayer.

Doden, W. **The semiology of retinal periphlebitis.** Klin. Monatsbl. f. Augenh. **137**:328-334, 1960.

The semiology of retinal periphlebitis is described on the basis of a study of 730 cases. It occurred in three times as many men as women in this series. The average age of onset was 30 years. In 70 percent of the patients both eyes were affected. The author distinguishes predominantly exudative, hemorrhagic, or proliferating forms. Partial or total retinal detachment occurred in 13 percent of the diseased eyes. A rational therapy of retinal periphlebitis is as unknown as the etiology. (1 table) F. H. Haessler.

Filho, A. and Giardulli, A. **Surgical treatment of retinal detachment.** Rev. brasil. oftal. **19**:295-310. Dec., 1960.

The authors present the important steps in the treatment of retinal detachment schematically by means of tables. They emphasize the importance of preoperative bed rest, exact localization of tears, the different surgical methods available, the postoperative course and possible complications, as well as recurrences of the detachment. (8 tables) Walter Mayer.

Gärtner, J. **Clinical and histologic observations on preformed ora-parallel structures of the limiting membrane of the vitreous.** Klin. Monatsbl. f. Augenh. **137**: 273-285, 1960.

The author points out that such changes do not only occur as a result of equatorial degeneration and describes some clinical examples, namely: two cases of a strip of blood accompanying periphlebitis, one an expression of scarring with periphlebitis, and one with questionable angiomatosis of the retina or Leber's miliary aneursym. (10 figures, 8 references) F. H. Haessler.

Hisatomi, C. **Studies on the retinal vascular caliber by means of fundus photomicrometry.** Acta Soc. Ophth. Japan **64**: 2572-2592, Oct., 1960.

Hisatomi obtained a curve by a measurement in the fundus photograph which shows the change in the vessel caliber corresponding to the distance from the disc (caliber-distance curve). The retinal vessels increase their caliber after they leave the disc. Arteries reach the greatest caliber at the point 600 μ from the disc and the veins 400 μ from the disc. In angiosclerosis the vessel caliber at a certain point has little meaning but the change in the form of the caliber-distance curve gives a definite indication. In angiosclerosis the curve becomes flat in the area up to 800 μ (artery) and 600 μ (vein) from the disc, and becomes steep thereafter. (30 figures, 22 tables, 27 references) Yukihiko Mitsui.

Jesberg, D. O. and Schepens, C. L. **Retinal detachment associated with coloboma of the choroid.** A.M.A. Arch. Ophth. **65**:163-173, Feb., 1961.

Thirteen cases of choroidal coloboma were found among the records of 9900 patients. Retinal detachment was observed in ten eyes of seven patients. Diathermy must be done with great care because these eyes respond poorly to any surgical trauma (10 figures, 6 references) Edward U. Murphy.

Klemens, Fritz. **Experiences and therapeutic possibilities with application of a plastic cylinder to the globe.** Klin. Monatsbl. f. Augenh. **137**:222-232, 1960.

A report is given on 125 cases of retinal detachment which had been operated on by means of scleral buckling. A variation of the method of Custodis consisting in the employment of long plugs covering several quadrants is discussed. The use of the latter for the purpose of blocking whole quadrants is recommended on account of the results achieved with this method. The objections raised against

scleral buckling are critically considered and the possibilities of avoiding these complications are pointed out. (2 figures, 6 tables, 6 references)

Author's summary.

Landau, J. and Halevi, H. S. **Incidence of glaucoma in various ethnic groups in the population of Israel.** Brit. J. Ophth. 44:751-754, Dec., 1960.

The oriental Jews living in Israel have a higher incidence of glaucoma than those from Europe. There are no sex differences. (2 tables, 7 references) I. E. Gaynon.

Lieb, W. A., Geeraets, W. J. and Guerry, D. **Retinopathy in sickle-cell disease.** Klin. Monatsbl. f. Augenh. 137:60-72, 1960.

The clinical picture of sickle-cell disease and the different electrophoretic subforms are discussed and illustrated by figures and tables. The importance of this disease in southern latitudes is underlined.

The fundus changes are divided in four grades on the basis of 65 cases, similar to those of diabetic retinopathy, and named sickle-cell retinopathy. A correlation of sickle-cell retinopathy with the general clinical picture of the disease is done. An explanation of the pathogenesis of the fundus changes is tried. Therapeutic measurements are discussed. (14 figures, 2 tables)

The very extensive bibliography may be had from Klin. Monatsbl. by request:

Dr. W. A. Lieb, Univ.Augenklinik, (16) Frankfurt a. M. -Süd 10, Ludwig-Rehn Str. 14;

Dr. W. J. Geeraets and Dr. D. Guerry, 1200 E-Broad Street, Richmond, Va.

Author's summary.

Madroskiewicz, M. **Improved calibrated electrodes for diathermy operations in retinal detachment.** Brit. J. Ophth. 44:698-699, Nov., 1960.

The author briefly describes two calibrated electrodes for use in penetrating and nonpenetrating diathermy procedures in retinal detachment. The electrodes are placed on a long arm that reaches around the curvature of the sclera. (2 figures, 1 reference) Morris Kaplan.

Otto, J. **The treatment of diabetic retinopathy with fructose.** Klin. Monatsbl. f. Augenh. 137:176-193, 1960.

In the organism fructose is utilized partially or entirely independent from insulin. Therefore there is a possibility to administer fructose to the diabetic as an additional source of energy without the risk of disturbing the sugar balance of the organism. Since fructose metabolism is taking place practically in the liver only, the capacity of the liver for fructose has to be considered. Thus the following rules for treatment result: 1. Generally the amount of fructose administered should not exceed 60 to 80 gm. per day. 2. By no means fructose should be administered in great doses all at once, it rather has to be given in amounts distributed equally over the day. As to the mode of administration, fruit juice sweetened with fructose has proved useful. The latter is taken by the patients in sips distributed over the day between meals. In patients with diabetic retinopathy a consequent treatment with fructose for a period of many months revealed that an essential improvement of the diabetic retinal affection can be achieved by means of this therapy. (10 figures, 11 references)

Author's summary.

Velicky, J. and Kellen, J. **Accessory studies in periphlebitis retinalis.** Klin. Monatsbl. f. Augenh. 137:335-342, 1960.

The authors examined 60 patients of whom 42 were men and 18 were women. One significant datum was that patients with the classic picture of retinal periphlebitis often have an increase in the quantity

of mucoprotein excreted into the urine. This manifestation was statistically confirmed to a probability stage of 0.1. This finding is useful as a support to a diagnosis of periphlebitis retinalis. (1 table, 10 references) F. H. Haessler.

Yamashita, T. and Cibis, P. **Experimental retinitis proliferans in the rabbit.** A.M.A. Arch. Ophth. **65**:49-58, Jan., 1961.

Intravitreal injection of autogenous blood or of saccharated iron oxide produces retinitis proliferans in the eyes of rabbits. In 11 of 13 eyes of diabetic patients, iron was found deposited in the proliferated tissue. These findings suggest that iron itself may play a role in the development of diabetic retinitis proliferans. (12 figures, 2 tables, 9 references)
Edward U. Murphy.

Zehetbauer, G. **Investigations on the antibacterial properties of the human vitreous.** Klin. Monatsbl. f. Augenh. **137**: 747-752, 1960.

The author repeated experiments by Shafer, Bussey, and Reed, according to whose publications the human vitreous has self-sterilizing properties. Vitreous was removed under sterile conditions from eight cadaver eyes. Pseudomonas aeruginosa was cultured from one sample. The remaining specimens were infected with Staphylococcus aureus, Escherichia coli, and Pseudomonas aeruginosa and kept at a temperature of +4°C. The self-sterilizing effect was observed after two to six days. Five out of seven specimens also inhibited bacterial growth on blood agar plates. The author surmises that the so-called self-sterilizing effect of the vitreous body is due to its content of antibiotics, which were taken by the patients prior to death; this effect was absent when no such medication was administered. (2 tables, 9 references)
Gunter K. von Noorden.

12
OPTIC NERVE AND CHIASM

Barontini, F. and Fossi, G. **Leber's disease: with two case reports.** Riv. oto-neuro-oftal. **35**:375-382, July-Aug., 1960.

The authors describe two patients in whom a diagnosis of Leber's disease was made. Hereditary factors in optico-chiasmatic arachnoiditis are discussed. (3 figures, 22 references)
Wm. C. Caccamise.

Fontes, R. **Treatment of optic neuritis.** Rev. brasil. oftal. **19**:323-340, Dec., 1960.

The author reviews the entire subject of optic neuritis and concludes that for better treatment it is essential to have a greater knowledge of its etiology. He classifies the latter into toxic, general infectious, and focal infectious factors.

The symptomatic treatment may be medical antiinfectious, antiallergic and antiinflammatory or surgical. The latter may be surgery on the vascular plexus and surgery in which the optic nerve is dissected free from its surroundings. (44 references) Walter Mayer.

Ikui, H. and Mimatsu, T. **The pathogenesis of optic nerve sheath hemorrhage.** Acta Soc. Ophth. Japan **64**:1777-1790, Aug., 1960.

In necropsy of six hypertensive individuals a hemorrhage was found around the optic nerve. This report deals with histologic analysis of this kind of hemorrhage. The hemorrhage was found in the optic nerve, its heath and the intervaginal, intradural, intraneural, and subdural spaces. In three of the six cases necrotic foci in the nerve fibers of the optic nerve were found. A demyelination was demonstrated at a distal portion adjacent to an intervaginal hemorrhage. The authors emphasize the observation that a hemorrhage in the optic nerve is not rare and is as important as retinal hemorrhage in hyper-

tensive persons. (24 figures, 2 tables, 10 references) Yukihiko Mitsui.

Neumann, P. S., Kaplan, A. and Brodsky, M. E. **Glioma of the optic nerve.** Arch. oftal. Buenos Aires **35**:279-283, Aug., 1960.

The case of a four-year-old boy is reported in whom an extensive fibrilar astrocytoma affecting both the intraorbital and intracanalicular portions of the optic nerve was removed by the transcranial route. The eye was left in place, and in spite of the complete excision of the optic nerve it presented a normal appearance at the end of one year. (5 figures, 11 references) A. Urrets-Zavalía, Jr.

Raimondo, N. **Enlarged blind spot without papilledema.** Riv. oto-neuro-oftal. **35**: 288-297, May-June, 1960.

Normally the perimetrist thinks of papillo-retinal edema when he is confronted by an obvious enlargement of the blind spot, although this may also result from a posterior staphyloma or a persistence of myelinated nerve fibers about the disc. In all of these conditions there are positive ophthalmoscopic findings. In this article the author stresses enlargement of the blind spot without ophthalmoscopic evidence of papilledema or other fundus pathology or variations that could lead to enlargement of the blind spot. A syndrome with this tangent screen finding was described in 1957 by Dubois-Poulsen-Magis. The author presents eight case histories of this syndrome. The syndrome is characterized by bilateral enlargement of the blind spot with a tendency to involvement of the temporal field. It is most commonly found in patients with lesions in the region of the chiasm together with compression of the anterior ventricular system. (8 figures, 2 references)

Wm. C. Caccamise.

Raimondo, N. and Romagnoli, M. A. **Problems of differential diagnosis in optic atrophy associated with nasal field defects.** Riv. oto-neuro-oftal. **35**:262-287, May-June, 1960.

The authors discuss optic atrophy with nasal field defects in relationship to the following conditions: 1. glaucoma in which the tension is slightly elevated, elevated only through provocative tests or absent altogether (pseudoglaucoma or soft glaucoma); 2. the syndrome resulting from direct compression of the ocular nerve either by a vessel or a tumor; 3. arteriosclerotic optic atrophy; 4. syphilitic optic atrophy; and 5. optico-chiasmatic arachnoiditis. Case reports of each type of etiological basis are presented. (6 figures, 25 references) Wm. C. Caccamise.

13

NEURO-OPHTHALMOLOGY

Miller, D. and Bleazel, K. F. **A study of subdural haematoma.** M. J. Australia, **2**: 1034-1037, 1960.

A consecutive series of 64 cases of subdural hematoma comprised two distinct pathological entities with no evidence of a link between them; namely 1. the classical chronic subdural hematoma of a fluid enclosed in a membrane, and 2. subdural clots due to severe trauma with brain laceration and primary hemorrhage into the subarachnoid space. In the latter there was no typical membrane formation.

Ocular signs are described and include palsies of the third cranial nerve (with or without dilatation of the pupil). Papilledema was present in nine cases.

Ronald Lowe.

Sogg, R. L. **Congenital facial diplegia syndrome of Möbius.** A.M.A. Arch. Ophth. **65**:16-19, Jan., 1961.

A typical case of this condition is described which supports the hypothesis that the anatomic defect is in the nuclei of the brain stem. (4 figures, 8 references)

Edward U. Murphy.

14

EYEBALL, ORBIT, SINUSES

Del Castillo, Caballero. **Orbital periostitis.** Arch. Soc. oftal. hispano-am. **20**: 420-423, May, 1960.

This is a report of a case of orbital cellulitis secondary to periostitis of the malar bone in a man who presented himself with a right unilateral exophthalmos of 15 days duration. It was not pulsating, there was no fever, pain or tenderness. The only abnormal feature of an exhaustive general examination was an eosinophilia. There was no response to treatment with antibiotics and sulfanamides. As the exophthalmos was progressing, a neoplasm was suspected and the patient was submitted to a thorough surgical exploration of the right orbit. The malar bone was found abnormal, and a piece of it removed for biopsy led to the diagnosis of periostitis of the malar bone. The final diagnosis was orbital cellulitis secondary to periostitis of the malar bone. Recovery was slow but complete with gradual recession of the exophthalmos. (2 figures)

Ray K. Daily.

Gass, J. D. M. **Acute orbital mucormycosis.** A.M.A. Arch. Ophth. **65**:214-220, Feb., 1961.

This syndrome has been described as characterized by uncontrolled diabetes, unilateral ophthalmoplegia, proptosis, meningoencephalitis, and rapid death. The responsible agent is an ordinarily saprophytic fungus which infects the nasal tissues and spreads rapidly backward. Only five of the 29 patients reported have survived and four of these were treated with systemic antifungal agents. Of the two patients reported here, one who was treated with amphotericin-B survived and the other, treated before these drugs were available, died. (5 figures, 21 references)

Edward U. Murphy.

Heath, W. E. **Buphthalmos over three generations.** Brit. J. Ophth. **44**:696-697, Nov., 1960.

A female infant was found to have typical buphthalmos and it was found that her father and grandfather had the same condition. This report adds substance to the belief in a genetic basis of this disease. (4 references)

Morris Kaplan.

Vancea, P. and Dobrescu, G. **Chronic orbital myositis of undetermined nature.** Arch. d'ophth. **20**:711-722, Oct.-Nov., 1960.

The authors present an anatomico-clinical study of two cases of chronic orbital myositis, a rare disease characterized in all reported cases by a palpebral edema, dilatation of the episcleral and conjunctival vessels, and an irreducible, painless exophthalmos. Ocular movements are restricted early in the disease and sometimes there is retraction of the upper lid due to hypertonicity of the levator. The two reported cases are described in detail and the microscopic findings are documented by seven photomicrographs which illustrate the principal findings: polymorphous infiltration of the muscles with granular degeneration of the fibers, and complex vascular lesions with orbital phlebitis predominating. (8 figures, 19 references)

P. Thygeson.

15

EYELIDS, LACRIMAL APPARATUS

Busse-Grawitz, Ernst Günther. **The pus cells of leukemic patients.** Arch. f. Ophth. **162**:500-510, 1960.

Lacrimal fluid of patients with leukemia of one type or another was examined cytologically several hours after instilling a drop of silver nitrate solution into the cul-de-sac. The normal response by production of leukocytes was found disturbed quantitatively and morphologi-

cally, though unrelated to the corresponding blood picture. (4 figures, 15 references) Harri H. Markiewitz.

Irvine, R. S. **Buried rubber tubes in nasolacrimal duct stenosis.** A.M.A. Arch. Ophth. **65**:192-195, Feb., 1961.

Two types of buried rubber tubes were used by the author over ten years ago in procedures to restore intranasal drainage from the conjunctival sac. Fifteen patients were so treated with no serious reactions and no failures. (3 figures, 11 references)
Edward U. Murphy.

Theodore, F. H. **Annual reviews. Lids, lacrimal apparatus, and conjunctiva.** A.M.A. Arch. Ophth. **65**:130-158, Jan., 1961.

The significant literature for the last half of 1959 and the first half of 1960 is discussed. (160 references)
Edward U. Murphy.

16
TUMORS

Dabezies, O. H., Walsh, F. B. and Hayes, G. J. **Papilledema with hamartoma of hypothalamus.** A.M.A. Arch. Ophth. **65**:174-180, Feb., 1961.

This is the eighteenth reported case of hamartoma of the hypothalamus and the first with ocular changes. Marked exudative retinopathy with papilledema was found bilaterally. Decreased vision was the presenting symptom. (6 figures, 1 table, 24 references)
Edward U. Murphy.

Goldberg, B., Tabowitz, D., Kara, G. B., Zavell, S. and Espiritu, R. **The use of P^{32} in the diagnosis of ocular tumors. I. A clinical report of 125 cases.** A.M.A. Arch. Ophth. **65**:196-211, Feb., 1961.

Experience with isotope studies over a 30-month period showed only two false results in 37 positive studies. None of the negative results have been invalidated to date. This test provides considerable aid in differentiating malignant from benign ocular lesions and also in the management of blind eyes with opaque media. (13 figures, 2 tables, 16 references)
Edward U. Murphy.

Hermann, P., Hervouet and Lenoir. **Cancer of the retina and irradiation.** Arch. d'opht. **20**:706-710, Oct.-Nov., 1960.

The authors have had the unique opportunity of obtaining an eye with retinoblastoma which appeared to have been treated successfully with irradiation. The tumor, in a female infant, was discovered in the left eye at two months of age and the eye was enucleated. At this time the right eye appeared to be normal. Sixteen months later a tumor was discovered in the right eye and was exposed to a total of 4,000 r in two doses, followed by a third dose of 2,000 r two months later. The tumor regressed and was considered healed. Death occurred from a tumor of the floor of the third ventricle. Examination of the right eye showed that the tumor had not healed and that two foci not observed clinically were present. The findings are described in detail with seven photomicrographs. (7 figures)
P. Thygeson.

Kesavachar, K. R. and Junnarkar, R. V. **Diktyoma.** Brit. J. Ophth. **44**:693-695, Nov., 1960.

Diktyoma is the name given to a neoplasm of the ciliary epithelium in children which may be benign or may be invasive and highly malignant. The authors describe a six-year-old child who had a cystic mass in the posterior chamber. This was drained from the outside but a severe iridocyclitis developed which necessitated enucleation. Histologic study revealed a

circumscribed tumor arising from the ciliary body with numerous partially calcified islets of cartilage. It had a framework of connective tissue but no organized stroma. (2 figures, 7 references) Morris Kaplan.

18

SYSTEMIC DISEASE AND PARASITES

Burian, H. M. **Note on the electroretinogram in a case of macroglobulinemia and some forms of anemia.** A.M.A. Arch. Ophth. **65**:111-113, Jan., 1961.

Preliminary results are reported in cases of macroglobulinemia, aplastic anemia, secondary anemia, Cooley's anemia, and hemolytic anemia. (2 figures, 3 references) Edward U. Murphy.

Coyle, J. T., Frank, P. E., Leonard, A. L. and Weiner, A. **Macroglobulinemia and its effect upon the eye.** A.M.A. Arch. Ophth. **65**:75-80, Jan., 1961.

A 46-year-old patient showed the funduscopic picture of central retinal vein occlusion and was found to have macroglobulinemia and leukemia. Plasmaphoresis resulted in marked visual improvement and resolution of ocular hemorrhages. This suggests that the fundus changes may be due to stasis rather than thrombosis. (3 figures, 12 references)
Edward U. Murphy.

Crawford, B. **Basilar embolism.** Brit. J. Ophth. **44**:689-692, Nov., 1960.

Occlusion of the internal carotid artery in the neck results in ischaemic changes in the eye which are being recognized with increasing frequency as the cause of field changes, monocular blindness or contralateral homonymous hemianopsia. Complete occlusion of the basilar artery from thrombosis leads to coma, quadriplegia, blindness and death; if the occlusion is incomplete a wide variety of symptoms may result.

A 62-year-old man noted severe headache and sudden complete blindness. He had had heart disease for 12 months previously and at the time had moderate to severe general hypertension. Pupillary light reflexes remained normal. With anticoagulant therapy his vision rapidly improved to normal. It is probable that an embolus which had originated in the heart occluded the basilar artery. (5 references)
Morris Kaplan.

Escribano, J. and Gonzales-Marin, P. **Takayashu's disease and ischemic ophthalmopathy.** Arch. Soc. oftal. hispano-am. **20**:405-416, May, 1960.

This is a comprehensive review of the literature on pulseless disease and the report of a case in a woman 35 years old. She had the syndrome typical of supraaortic vascular obliteration. She was operated for a cataract of one eye, with a successful surgical result but with little improvement in vision. (4 figures, 32 references) Ray K. Daily.

Garcia-Alix, Carlos. **A case of Takayashu disease.** Arch. Soc. oftal. hispano-am. **20**:401-404, May, 1960.

A case of pulseless disease is reported in a man 35 years of age; he had the classical symptoms of absence of pulse in the upper extremities, hypersensitivity of the carotid sinus, and changes in the fundus. The literature on the pathogenesis of the fundus lesions is reviewed and their similarity to those of retinopathy of prematurity is pointed out. (19 references)
Ray K. Daily.

Hanno, H. A. and Weiss, D. I. **Hypoparathyroidism, pseudohypoparathyroidism, and pseudo-psuedohypoparathyroidism.** A.M.A. Arch. Ophth. **65**:238-242, Feb., 1961.

The clinical and pathologic features of this triad of uncommon but related dis-

eases are described. (1 table, 31 references) Edward U. Murphy.

Jütte, A. **Fundus changes in acute visceral lupus erythematosus.** Klin. Monatsbl. f. Augenh. **137**:765-772, 1960.

Cotton-wool patches, flame-shaped hemorrhages, papilledema, and venous congestion were observed in the fundus of an 18-year-old female patient with disseminated lupus erythematosus. It is attempted to explain the pathogenesis of these fundus changes. (3 figures, 22 references) Gunter K. von Noorden.

Morello, A. and Cucco, G. **Arteriographic and ophthalmodynamometric findings in a patient with spontaneous recovery from carotid—cavernous fistula.** Riv. oto-neuro-oftal. **35**:383-392, July-Aug., 1960.

The authors present the case history of a 39-year-old woman in whom spontaneous recovery from a carotid—cavernous fistula occurred. Subjective symptoms were referred to the left side of the head and there was the objective finding of anisocoria with dilatation of the left pupil. The left eye also had dilatation of the papillary veins together with spontaneous venous pulsation. The corneal reflex was sluggish. There was paralysis of the left lateral rectus muscle and diplopia on looking laterally towards the left. There was a left exophthalmos which could not be reduced and was nonpulsating. Ophthalmodynamometry revealed a markedly reduced reading in the left eye. Electroencephalographic findings were within normal limits. Arteriography confirmed the clinical diagnosis of an aneurysmal sac in the intracavernous portion of the carotid artery. Spontaneous recovery occurred. (3 figures, 24 references)

Wm. C. Caccamise.

Silanos, G. and VonBerger, G. P. **Foster Kennedy syndrome occurring in a tuberculous meningitis.** Riv. oto-neuro-oftal. **35**:513-519, Sept.-Oct., 1960.

The authors describe the findings in a 15-year-old girl who had partial atrophy of the right optic disc and papilledema of the left. Spinal fluid studies confirmed the impression of tuberculous meningitis. The authors emphasize the importance of combined antibiotic and steroid therapy, particularly by intrathecal injection in such patients. (2 figures, 9 references)

Wm. C. Caacamise.

Sutherland, J. M., Tyrer, J. H. and Eadie, M. J. **The clinical features of multiple sclerosis.** M. J. Australia, **1**:49-53, 1960.

Multiple sclerosis is not uncommon in Queensland. An analysis of some clinical features in a series of 558 patients is presented. The incidence and types of ocular disturbance resemble those reported from Great Britain. (6 tables) Ronald Lowe.

Timm, G. **Pathological anatomy of the eye in macroglobulinemia Waldenstroem.** Klin. Monatsbl. f. Augenh. **137**:772-781, 1960.

A 55-year-old male patient died of macroglobulinemia. The eyes were obtained and a detailed histological description is given. The most outstanding features are: severe lymphoid-plasma cellular reaction of the anterior and posterior uvea, exudates, hemorrhages, microthrombi, and retinal detachment caused by retroretinal hemorrhages. (10 figures, 23 references)

Gunter K. von Noorden.

19

CONGENITAL DEFORMITIES, HEREDITY

Grove, J. H., Shaw, M. W. and Borque, G. **A family study of aniridia.** A.M.A. Arch. Ophth. **65**:81-93, Jan., 1961.

The author examined the eyes of 40 persons who had aniridia and were members of one of the seven generations of

this family in which 77 individuals were known to have this defect. Cataracts were found in every one over 10 years of age but only 10 had glaucoma. The great majority eventually became blind. (1 figure, 5 tables, 14 references)

Edward U. Murphy.

Lumbroso, B. **A case of congenital bilateral paralysis of the facial and adductor nerves together with ptosis.** Riv. otoneuro-oftal. **35**:408-414, July-Aug., 1960.

The author presents the record of a 13-year-old boy with congenital ptosis and divergent strabismus of 100 prism diopters for distance and near. There was only a vague suggestion of adduction. A bilateral facial paralysis was also present. A review of the literature is presented. (21 references) Wm. C. Caccamise.

Rogers, J. W. **Ankyloblepharon filiforme adnatum.** A.M.A. Arch. Ophth. **65**: 114-117, Jan., 1961.

A case of this abnormality associated with other congenital mesodermal defects developing in the eighth to the ninth fetal week is reported. Microscopic examination of the lids showed no abnormalities except for the presence of connective tissue bands containing blood vessels and covered by epithelium. (1 figure, 12 references) Edward U. Murphy.

Veirs, E. R. and Brown, W. **Congenital miosis.** A.M.A. Arch. Ophth. **65**:59-60, Jan., 1961.

This condition was observed in four individuals three of whom are related and in consecutive generations. One patient had glaucoma which did not respond to peripheral iridectomy or drug therapy. Shallow anterior chambers and abnormally placed iris tissue resembling that in lower placentals were noted. (3 references) Edward U. Murphy.

20

HYGIENE, SOCIOLOGY, EDUCATION, AND HISTORY

Feigenbaum, A. **Did "Ali Ibn Isa" use general anesthesia in eye operations?** Brit. J. Ophth. **44**:684-688, Nov., 1960.

Ali Ibn Isa was an Arab oculist of the tenth century who wrote a treatise on ophthalmology in which later translators found that surgery was done under general anesthesia. In one key Arabic work a passage which was translated as "sending a person to sleep" in reality meant having the person lie down. The early surgical procedures were performed on a patient who was recumbent rather than asleep. (9 references) Morris Kaplan.

Mora Calvo-Flores, Francisco. **Epidemiology of trachoma.** Arch. Soc. oftal. hispano-am. **20**:347-391, May, 1960.

This is the report of an investigation conducted in the southeast of Spain by the health department with the assistance of the World Health Organization and UNICEF. The material for the analysis comprises 2,680 persons infected with trachoma. They were examined with a hand slitlamp and a magnifying lens. The records and diagnostic criteria utilized were those established by the Expert Committee on trachoma. The report is statistical and graphic. The photographs convey the atmosphere of poverty, under which this disease flourishes. (16 tables, 13 photographs) Ray K. Daily.

NEWS ITEMS

EDITED BY DONALD J. LYLE, M.D.
411 Oak Street, *Cincinnati, Ohio*

News items should reach the editor by the 10th of the month. For adequate publicity, notice of postgraduate courses and meetings should be received three months in advance.

ANNOUNCEMENTS

COLORADO CONVENTION

The subject for discussion at the annual postgraduate course in ophthalmology of the University of Colorado School of Medicine and the summer convention of the Colorado Ophthalmological Society will be "External ophthalmology." The meeting will be held at the Stanley Hotel, Estes Park, Colorado, on July 10th through 13th. Guest speakers will be Dr. Raynold N. Berke, New York; Dr. Frederick C. Blodi, Iowa City; Dr. Ramon Castroviejo, New York; and Dr. Frank W. Newell, Chicago. Representing the faculty of the University of Colorado School of Medicine will be Dr. C. Wesley Eisele, dean in charge of postgraduate medical education; Dr. Philip P. Ellis, head of the Department of Ophthalmology; Dr. Morris Kaplan, Dr. Richard C. Vanderhoof and Dr. Robert L. Weiner. The registration fee is $60.00 payable to the University of Colorado School of Medicine. For further information write the Office of Postgraduate Medical Education, University of Colorado Medical Center, 4200 East Ninth Avenue, Denver 20, Colorado.

SOUTHERN MEDICAL ASSOCIATION PAPERS

The Section of Ophthalmology and Otolaryngology of the Southern Medical Association announces that now being accepted are papers by physicians of either specialty living in the area of the Southern Medical Association for consideration for presentation at the next annual meeting to be held in Dallas, Texas, from November 6th to 9th.

The paper or an abstract of the paper should be sent directly to the Secretary, Dr. Albert G. Esposito, Suite 1212, First Huntington National Bank Building, Huntington, West Virginia, as soon as possible.

MEDICAL STAFF SYMPOSIUM

The Memorial Hospital of Long Beach, California, announces its third annual medical staff symposium to be held at Memorial Hospital, 2801 Atlantic Avenue, Long Beach 6, California. Henry Brainerd, M.D., chairman, Department of Medicine, University of California School of Medicine, San Francisco, will be the guest speaker. For further information write George X. Trimble, M.D., secretary, Memorial Hospital of Long Beach, California.

SOCIETIES

MIDWESTERN SECTION

The Midwestern Section of the Association for Research in Ophthalmology met at the University of Kansas Medical Center, Kansas City, Kansas, on April 29th and 30th.

PITTSBURGH MEETING

The 11th annual clinical meeting of the Eye and Ear Hospital, Pittsburgh, was held on April 19th. On the ophthalmology program were: "Tumors of the lids and their surgical treatment," Dr. M. Noel Stow, Washington, D.C.; "Symposium on lid surgery," Dr. Murray F. McCaslin, moderator; Drs. M. Noel Stow, Franklin D. Hoffman and Joseph F. Novak; "The A and V syndromes: Altering the height of the insertions of the horizontal rectus muscles," Dr. Philip Knapp, New York; "Symposium on problems of motility," Dr. Jay G. Linn, Jr., moderator; Drs. Philip Knapp, Robert W. Saul, George R. Geeseman and John C. Dunbar.

KANSAS MEETING

On the eye program for the annual guest day meeting of the Kansas City Society of Ophthalmology and Otolaryngology were: "Neuro-ophthalmology," Dr. Edward W. D. Norton, "Strabismus," Dr. Marshall M. Parks; "Contact lenses," Dr. Louis J. Girard; "The ophthalmodynamometer," Dr. Larry L. Calkins; "Interesting eye lesions," Dr. Dick H. Underwood: Office management of glaucoma," Dr. Albert N. Lemoine, Jr.; "Low-tension glaucoma," Dr. Earl G. Padfield; "Diagnosis and management of intraocular foreign bodies," Dr. Truman B. Schertz; "Uveitis," Dr. James T. Robison, Jr.

MASSACHUSETTS EYE AND EAR

The annual meeting of the Massachusetts Eye and Ear Infirmary Alumni Association and of the New England Ophthalmological Society was held at the Infirmary on April 25th and 26th. Dr. Merrill J. King, president of the association, presided over the meetings of the ophthalmologic section. On the program were: "A brief review of recent advances in electroretinography," Dr. Benjamin Ziv, Boston; "More about retinal vessels," Dr. David G. Cogan, Boston; "Frozen donor material for lamellar keratoplasty," Drs. C. H. Dohlman and Edward C. Sweebe, Boston; "Operative procedure to prevent vitreous-block glaucoma following cataract surgery," Dr. Thomas Cavanaugh, Boston; "A case of bilateral uveitis with secondary glaucoma," Dr. C. Ray Franklin, New York; "Reformation of flat anterior chambers following filtering operations," Dr. John R. Gehring, Lowell,

Massachusetts; "The Gloucester preschool "lazy eye" test," Dr. Frederic B. Breed, Danversport, Massachusetts.

"Herpes simplex keratitis," Dr. Herbert E. Kaufman, Boston; "Massive uveal transundation: A new disease entity?" Drs. Charles L. Schepens and Robert J. Brockhurst, Boston; "A new fundus camera for taking simultaneous stereoscopic photographs," Dr. David D. Donaldson, Boston; "An office procedure for correction of entropion," Dr. Frederick B. Breed; "Synthetic tubes in glaucoma surgery," Drs. William Stone, Jr., and John Sebestyen, Boston; "Glaucoma secondary to scleral buckle," Dr. Taylor Smith, Boston; "Ocular symptoms with whiplash type of head and neck injury," Dr. David H. Scott.

At the 460th meeting of the New England Ophthalmological Society, a clinical conference was conducted by Dr. David D. Donaldson. Dr. Robert J. Brockhurst discussed "The differential diagnosis of retinal detachment," and Dr. Charles D. J. Regan, "Current scleral buckling technique." Other papers were: "The use of phospholine iodide in the management of esotropia," Dr. Kevin Hill and Miss Ann Stromberg; "A new trephine for keratoplasty," Dr. Benjamin Ziv; "The travelling ophthalmologist," Dr. Paul A. Chandler, Boston; and "Follow-up observations on the vitreous syndrome after cataract surgery," Dr. S. Rodman Irvine, Los Angeles.

NSPB MEETING

The 1961 conference of the National Society for the Prevention of Blindness was held at the Barbizon-Plaza Hotel, New York, April 12th through 14th. Subjects discussed at the conference were: "Conserving vision of the aging," "The values of low vision aids," "Advances in industrial vision conservation," "Ophthalmia neonatorum—decontrol?", "Building blocks for a better public relations program," "The partially seeing child: Guidance and counseling."

SECTION ON OPHTHALMOLOGY AMA

The Section of Ophthalmology will meet in the Terrace Room of the Plaza Hotel during the American Medical Association convention in New York, June 27th through June 29th. The first session will open at 9:00 A.M. on Tuesday, June 27th. On the program will be:

"Hypophyseal stalk section in the treatment of advancing diabetic retinopathy," Joel Contreras, Richard A. Field, William A. Hall and William H. Sweet, Boston; with the discussion to be opened by Samuel J. Kimura, San Francisco; "Penetrating keratoplasty in Fuchs' dystrophy," Daniel W. Doctor, Westport, Connecticut, and R. Townley Paton, New York, with discussion opened by Frederick W. Stocker, Durham, North Carolina, and E. M. Trayner, New York; "Nonviable donor material in lamellar corneal transplantation," Edward C. Sweebe and Claes H. Dohlman, Boston, discussion opened by John Harry King, Jr., Washington, D.C.

"Observations on superficial punctate keratitis: A specific type of epithelial keratitis," Phillips Thygeson, San Jose, California, discussion opened by Alson E. Braley, Iowa City; "Keratomycosis," Wendell D. Gingrich, Galveston, discussion to be opened by Ernest W. Chick, Durham; "The diagnosis and management of fungus endophthalmitis following cataract extraction," Frederick H. Theodore, Maxwell L. Littman and Ernesto Almeda, New York, discussion opened by Ben S. Fine, Washington, D.C.; "The treatment of acute optic neuritis: An analysis of 80 cases," Conrad L. Giles and J. D. Isaacson, Ann Arbor, Michigan, discussion opened by Frank D. Carroll, Rye, New York; "The ocular effects of whiplash injuries," Harry Horwich, Coral Gables, Florida, discussion opened by Herbert Wiesinger, Richmond, Virginia.

The meeting of the second day will convene at 9:00 A.M. The following papers will be presented: "Ophthalmodynamometry in the surgical management of carotid artery disease," Warren Lieberman and Robert A. Schimek, New Orleans, discussion opened by Robert W. Hollenhorst, Rochester, Minnesota; "Blackouts not obviously due to carotid occlusion," David G. Cogan, Boston, discussion to be opened by Frank B. Walsh, Baltimore.

"The physiological significance of gerontoxon, especially in younger individuals," John Finley, Haddonfield, Pennsylvania, and Donald Berkowitz, Philadelphia, discussion opened by David G. Cogan, Boston; "Ocular manifestations of leukemia and allied disorders," Raymond A. Allen and Bradley R. Straatsma, Los Angeles, discussion to be opened by Frank W. Newell, Chicago; "The management of metabolic malignant exophthalmos," Robert M. Sinskey, Santa Monica, California, discussion to be opened by Robert M. Day, New York.

Papers to be presented at the final session on Thursday June 29th at 9:00 A.M. are: "Chairman's address," Banks Anderson, Durham; Address of the invited guest, Victor A. McKusick, Baltimore, "Heritable disorders of connective tissue with eye involvement."

"Hereditary diseases of the eyelids," Harold F. Falls, Ann Arbor, discussion opened by Taylor Asbury, Cincinnati; "Uveal necrosis following retinal detachment surgery," Milton Boniuk and Lorenz E. Zimmerman, Washington, D.C., discussion opened by Taylor R. Smith, Boston.

A symposium on "Epinephrine therapy of glaucoma," will include: "Improvement of the coefficient of outflow in glaucomatous eyes during prolonged local treatment with epinephrine," Elmer J. Ballintine, Cleveland, and Lawrence L. Garner, Milwaukee; "Topical epinephrine therapy of open-angle glaucoma," Bernard Becker, Thomas H. Pettit and Andrew J. Gay, Saint Louis; "A new epinephrine for glaucoma therapy," Daniel Vaughan, San Jose, Robert Shaffer and Sidney Riegelman, San Francisco. The discussion will be opened by Peter C. Kronfeld, Chicago.

WEST VIRGINIA ACADEMY

The West Virginia Academy of Ophthalmology

and Otolaryngology met at the Greenbrier Hotel, White Sulphur Springs, West Virginia, on April 6th through 8th. Guest speakers were Dr. Harvey E. Thorpe, Pittsburgh, and Dr. Irving H. Leopold, Philadelphia.

Mexican society officers

Elected as officers of the Mexican Ophthalmological Society are: President, Renán Murillo Fajardo; vice president, Armando Ramírez; secretary, Sabino Silva Zerón; secretary, Raúl A. Chavira; treasurer, Roberto Wallentín; committee on honors: Antonio Torres Estrada, Lino Vergara Espino and Luis Sánchez Bulnes; committee on admissions: Enrique Graue, Abelardo Zertuche, and Enriqueta Camacho; directors: Sergio Chavira and Magín Puig Solanes.

Carolinas meeting

The joint annual meeting of the North Carolina Eye, Ear, Nose and Throat Society and the South Carolina Society of Ophthalmology and Otolaryngology will be held at the Francis Marion Hotel, Charleston, South Carolina, on September 11th and 12th. An excellent program has been arranged. There will be three guest ophthalmologists and three guest otolaryngologists. There will be entertainment features for both the physicians and ladies.

Long Island meeting

At a recent meeting of the Long Island Ophthalmological Society, Mr. Harold Shapiro, a representative for the State Insurance Fund, spoke on "The lawyer looks at ophthalmolic malpractice." His paper was discussed by Dr. Jack Lisman.

Central Illinois program

The 36th convention of the Central Illinois Society of Ophthalmology and Otolaryngology was held recently at the Abraham Lincoln Hotel, Springfield, Illinois. On the program were: A moving picture film by Dr. Karl Hruby of Graz, Austria, on "Enzymatic zonulolysis," presented by Dr. E. C. Albers, Champaign; "The management of exodeviations," Dr. Arthur Jampolsky, San Francisco; "Strabismus: Surgical criteria and principles," Dr. Jampolsky.

United Kingdom meeting

The 81st annual congress of the Ophthalmological Society of the United Kingdom was held recently in London. Papers presented included: A symposium on "The late complications of aphakia," speakers: Mr. A. J. B. Goldsmith, Mr. J. R. Hudson, and Mr. L. E. J. Werner; "Experimental work on the effect of trypsin on the cornea of the rabbit," Drs. Henri Miller and A. Brini; "Iris atrophy in primary glaucoma," Mr. J. Winstanley; "Remarks on spasms and tics in ophthalmic practice with notes on four cases of the syndrome of Gilles de la Tourette," Mr. L. H. Savin; Heterochromic uveitis," Mr. E. S. Perkins; "Impairment of wound healing after zonulolysis," Dr. R. J. McWilliam; "Nature of suprachoroidal fluid: Analysis, clinical findings and treatment in nine cases of postoperative choroidal detachment," Mr. J. H. Dobree.

Discussion on "Neovascularization in ocular disease," openers: Mr. Redmond Smith, Prof. Norman Ashton and Dr. A. G. Sanders; "The relationship between dark adaptation and visual field in glaucoma," Mr. E. G. Mackie, Dr. P. Chadwick and Dr. A. Jordan; "Clinical management of intraocular malignancy," Prof. E. B. Dunphy, Boston; "Ultrasonic rays in medical diagnosis," Dr. Douglas Gordon; "Vernal keratitis," Mr. Barrie R. Jones; "Capillary and cavernous hemangiomas of the orbit," Mr. H. E. Hobbs; "Phlebography as an aid to the diagnosis of orbital hemangiomas," Dr. G. H. Du Boulay.

"Simple eye photography," Mr. A. J. Ogg; "Hyaline degeneration of the conjunctiva, "Mr. M. J. Gilkes; "Three unusual cases," Dr. Peter Beattie; "Enucleation and terylene implant," Dr. Hugh O'Donoghue; "Visual assessment and visual defects in cerebral palsies in childhood," Mr. Joseph Minton.

The Bowman Lecture was presented by Miss Ida Mann whose subject was "Climates, cultures and eye diseases." Films on "Eye surgery of mass casualties without modern hospital facilities," and "Ciné dacryocystography," were presented by Dr. Roland I. Pritikin and Dr. Edward Epstein.

Miscellaneous

Moorfields anniversary

The Institute of Ophthalmology and Moorfields Eye Hospital, London, held an Open Day on Wednesday, April 12th, to mark the 150th anniversary of the founding of the teaching school.

Continuation course

The University of Minnesota conducted a continuation course in ophthalmology May 1st through 3rd. Dr. Phillips Thygeson, San Jose, California, and Dr. A. Edward Maumenee, Baltimore, were guest speakers. At the opening of the Ophthalmology Research Laboratory, Dr. V. Everett Kinsey, Detroit, and Dr. Harold G. Scheie, Philadelphia, were guest speakers.

Barcelona course

The third international course in ophthalmology of the Instituto Barraquer was held in the Avenida Palace Hotel, Barcelona, May 1st to 6th.

International eye-bank

Medico, Inc., the international medical-aid organization founded by the late Dr. Thomas A. Dooley, has established an international eye-bank with headquarters in Washington, D.C., to serve as a clearing house for the shipment of corneas for transplantation throughout the world.

Symposium on oculomotor system

At the Mount Sinai Hospital, New York, on April 14th and 15th was held on symposium on the oculomotor system supported by Grant #B-2539 from the National Institute for Neurological Dis-

eases and Blindness, United States Public Health Service. Papers included: "Introductory remarks," M. B. Bender, New York; "Cerebral oculomotor pathways," F. A. Mettler, New York; "Eye movements induced by electric stimulation of cerebrum in monkeys and their relationship to bodily movements," I. H. Wagman, New York; "Oculomotor functions in monkeys with lesions of the cerebrum and the superior colliculi," P. Pasik and T. Pasik, New York; "Oculomotor pathways defined by electric stimulation and lesions in the brain stem of monkey," M. B. Bender, New York, and S. Shanzer, Paris; "Interrelationship of brain stem and cortical areas for conjugate ocular movements in cats," Jane Hyde, Los Angeles.

Dr. R. B. Livingston, Bethesda, was chairman of the second session at which the following papers were read: "Oculomotor organization and proprioceptors to the eye muscles," R. Warwick, London; "Pathways and synaptic articulation patterns connecting vestibular receptors with oculomotor nuclei," J. Szentagothai, Budapest; "Vestibular connections in the brainstem," E. B. Gernandt, Bethesda; "Optovestibular integration in the visual cortex and the mechanism of nystagmus," H. H. Kornhuber, Freiburg, Germany; "Ocular movements related to lambda waves and sensitivity to visual patterns in man," R. G. Bickford, Rochester, Minnesota.

Dr. Lorrin Riggs, Providence, Rhode Island, presided over the session at which these papers were presented: "Eye movements in sleep," W. Dement, New York; "Some considerations of fusion in binocular vision and oculomotor imbalance," K. Ogle, Rochester, Minnesota; "Absence of conscious position sense in the eye," P. A. Merton, Cambridge, England; "Physiologic nystagmus and vision," R. M. Pritchard, Montreal, Canada; "Habituation of ocular nystagmus of vestibular origin," G. H. Crampton, Fort Knox, Kentucky.

At the final session, Dr. James O'Leary, Saint Louis, presided. Papers were: "Brain lesions and eye movements in man," David Cogan, Boston; "Results of electronystagmography in man: The value of optokinetic and vestibular nystagmus for neurologic diagnosis and research," R. Jung and H. H. Kornhuber, Freiburg, Germany; "Some recent work on the application of electronystagmography to certain diagnostic and other problems of otoneurology," C. S. Hallpike, London; "Spectrum analysis of the extraocular muscle electromyogram," G. Breinin, New York; "Gaps in our knowledge of oculomotor physiology," E. A. Spiegel, Philadelphia.

Personals

Dr. Frank W. Newell, Chicago, professor of ophthalmology and chairman of the Department of Ophthalmology, University of Chicago, recently attended the first meeting of the world-wide Problem Commission in Neuro-Ophthalmology, to which he was named a founding member from the United States. The meeting was held at Geneva, Switzerland.

Dr. Derrick Vail, Chicago, has been appointed a member of the International Council of Ophthalmology to replace one of the members who recently resigned. Dr. Vail will serve until the International Congress in New Delhi in 1962.

Dr. Charles I. Thomas has been appointed professor of ophthalmology and director of that division at University Hospitals, Western Reserve University, Cleveland.

Dr. Robert R. Trotter, Boston, has been appointed clinical associate professor of surgery and chairman of the Division of Ophthalmology, West Virginia University.

Dr. A. Benedict Rizzuti was guest speaker at the March meeting of the Pittsburgh Ophthalmological Society. He spoke on "Recent techniques in cataract and corneal surgery."

Dr. Irving Henry Leopold, chairman, Department of Ophthalmology, University of Pennsylvania Graduate School of Medicine, Philadelphia, spent the week of March 13th as a visiting professor of ophthalmology at the University of California School of Medicine in San Francisco. He conducted ward rounds and a number of clinics at which discussions of therapeutic problems were carried out. On Thursday morning he gave a lecture on "The anticholinesterase drugs" at the weekly staff conference, and that afternoon lectured on "Antibiotic therapy" at the weekly staff conference of the Proctor Foundation. On Friday evening he spoke before the San Francisco Ophthalmological Round-Table.

Dr. Sadi de Buen, associate professor of histology and pathology of the eye of the graduate course of ophthalmology of the University of Mexico Medical School, was named president of the Asociación Mexicana de Patólogos, A.C., for a two-year period, beginning in January 20, 1961.

URGENT REQUEST

The Uveitis Laboratory, University of California School of Medicine, San Francisco, is vitally interested in obtaining freshly enucleated eyes from patients with all types of uveitis and other endogenous inflammations. Attempts are being made to isolate etiologic agents from these eyes.

The eyes should be placed in a sterile bottle, packaged with the history and findings, and shipped as quickly as possible. Please send specimens special delivery, collect, and mark the package "Fresh Tissue Specimen—Rush." Do not freeze or use preservatives of any kind.

A report of isolations of organisms and pathologic findings, including a slide, will be sent to the contributor. Credit will be given in any resulting publications if desired.

Telegraph collect if specimen being sent.

Send eyes to

Samuel J. Kimura, M.D., Michael J. Hogan, M.D., or Phillips Thygeson, M.D.
University of California School of Medicine
San Francisco 22

Twenty-Seventh Annual Meeting
Postgraduate Medical Assembly of South Texas
July 10, 11, and 12, 1961—Monday through Wednesday
The Shamrock Hilton Hotel, Houston, Texas

OPHTHALMOLOGY PROGRAM

PAUL A CHANDLER, M.D.—Consulting Surgeon, Massachusetts Eye and Ear Infirmary, Boston, Mass.; Associate Clinical Professor of Ophthalmology, Harvard Medical School.

Subjects (1 hour each)

1. Open Angle Glaucoma Including Congenital Glaucoma, Monday, 9:00 a.m.
2. Angle Closure Glaucoma (1st session), Monday, 11:00 a.m.
3. Angle Closure Glaucoma (2nd session), Tuesday, 3:30 p.m.
4. Secondary Glaucoma (1st session), Wednesday, 9:00 a.m.
5. Secondary Glaucoma (2nd session), Wednesday, 11:00 a.m.

ARTHUR GERARD DEVOE, M.D.—Director of Institute of Ophthalmology of Presbyterian Hospital, New York City; Professor of Ophthalmology, College of Physicians and Surgeons, Columbia University, New York City.

Subjects (1 hour each)

1. Therapeutic Corneal Grafting, Monday, 10:00 a.m.
2. Lid Injuries, Tuesday, 2:30 p.m.
3. Injuries to the Globe, Tuesday, 4:30 p.m.
4. Hyphema, Wednesday, 10:00 a.m.

Registration fee of $25.00 includes all features: scientific program, exhibits, entertainment, luncheons, and special entertainment for the ladies.

Comparable program in Otolaryngology.

For further information, write Executive office, 412 Jesse H. Jones Library Building, Houston 25, Texas

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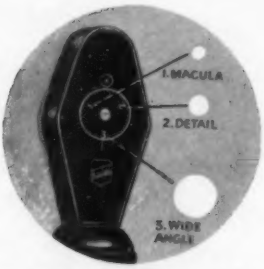

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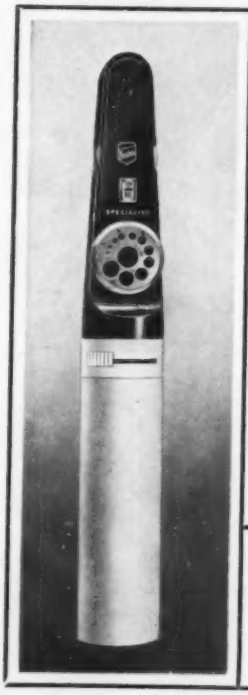

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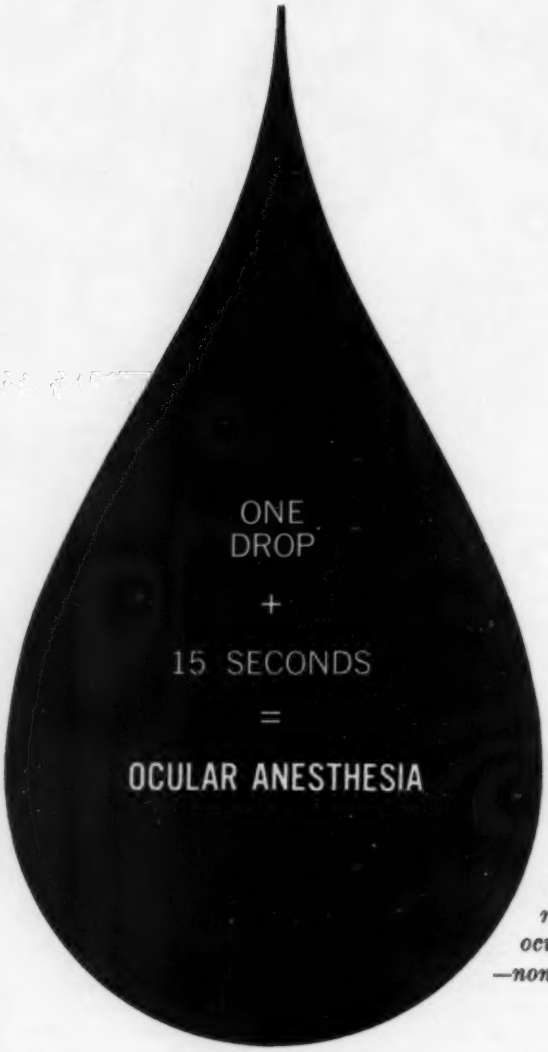

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Formula: Each 1 cc. contains:

Proparacaine HCl	0.5%
Chlorobutanol (Chloral deriv.)	0.2%
Benzalkonium chloride	1/10,000
Glycerin (as a stabilizer)	2.45%

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